J. Braz. Chem. Soc., Vol. 11, No. 5, 537-539, 2000.
Printed in Brazil

Short Report

Xanthones from *Vismia latifolia*

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Este trabalho relata o isolamento e a identificação de uma nova xantona, 1,4,8-triidroxixantona (1,4,8-triidroxi-9*H*-xanten-9-ona), isolada das raízes de *Vismia latifolia* (Guttiferae). Quatro outras xantonas conhecidas também foram isoladas: 1,5-diidroxi-8-metoxixantona, 1,7-diidroxixantona, 1,6-diidroxi-7-metoxixantona e 1,3,5,6-tetraidroxixantona, sendo as duas últimas inéditas no gênero *Vismia*. As estruturas foram estabelecidas através das técnicas de espectroscópicas de UV, IV, EM e RMN (1D e 2D).

A new xanthone,1,4,8-trihydroxyxanthone (1,4,8-trihydroxy-9*H*-xanthen-9-one), was isolated from the roots of *Vismia latifolia* (Guttiferae). Four other known xanthones were isolated: 1,5-dihydroxy-8-methoxyxanthone, 1,7-dihydroxyxanthone, 1,6-dihydroxy-7-methoxyxanthone and 1,3,5,6-tetrahydroxyxanthone. The last two compounds were isolated for the first time from a *Vismia* species. The structures were established by UV, IR, MS, 1D and 2D NMR spectroscopic techniques.

Keywords: *Vismia latifolia, Guttiferae,* 1,4,8-trihydroxyxanthone, xanthones

Introduction

Vismia latifolia Choisy (Syn. *Hypericum latifolium* Aubl.), a tree known popularly in Bahia (Brazil) as "pau-de-sangue", is used as a tonic and febrifugal agent[1]. This species belongs to the Guttiferae family, subfamily Hypericoideae and tribe Vismieae. Previous papers have reported the presence of anthranoids, terpenoids, flavonoids and xanthones from *Vismia* species[2-6]. As part of a chemotaxonomic study of the Guttiferae (*Vismia* genus), in the present paper we have identified the new compound 1,4,8-triidroxixantona (**1**) and four other known xanthones **2**, **3, 4** and **5** from *V. latifolia*. The last two compounds (**4** and **5**) were isolated for the first time in this genus. The occurrence of xanthones with a simple oxygenation pattern 1,4,8- (or 1,5,8-) in *Vismia* genus was described only in *V. guaramirense*[2] and *V. parviflora*[3].

Results and Discussion

Purification of an ethanol extract of the roots of *Vismia latifolia* by silica gel CC resulted in the isolation of a new trioxygenated xanthone 1,4,8-triidroxixantona (**1**). The molecular formula was deduced to be $C_{13}H_8O_5$ from its $[M]^+$ at *m/z* 244 in the mass spectrum and from the NMR spectra. A conjugated carbonyl group was identified by an absorption band at 1640 cm^{-1} in the IR spectrum[7]. The UV spectral data of **1** (experimental section) was characteristic of the xanthone chromophore[8] and the sodium acetate addition caused a batochromic shift; the consecutive addition of H_3BO_3 did not modify the UV spectrum, indicating the absence of the *ortho* hydroxyls. The ^{1}H NMR spectrum of **1** indicated the presence of signals corresponding to three aromatic hydrogens [d_H, 6.82 (dd, *J* 8.4 and 0.8 Hz, H-7), 7.05 (dd, *J* 8.4 and 0.8 Hz, H-5) and 7.76 (t, *J* 8.4 Hz, H-6)] in an ABC-type system due to 1,2,3-trisubstituted benzene ring, three hydroxyl groups [d_C 8.61 (s, HO-4), 11.05 (*s*, HO-1) and 11.83 (s, HO-8)] and two *ortho*-coupled hydrogens [d_H 6.70 (H-2) and 7.37 (H-3) (d, *J* 8.8 Hz)]. The ^{13}C NMR spectrum of **1** showed 13 carbon signals: eight non hydrogenated carbons, including one carbonyl group (d_C 187.53) and five methine aromatic carbons. These data (experimental section) suggested a trisubstituted xanthone (**1**). The unambiguous attribution was established by means of two-dimensional NMR spectroscopy techniques. The chemical shift assignments

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of methine carbons C-2, C-3, C-5, C-6 and C-7 in the ^{13}C NMR were achieved by a HMQC experiment [^1J(CH)]. The other chemical shifts were assigned by long-range [^2J(CH) and ^3J(CH)] correlation observed in the HMBC spectrum (Figure 1). Two possible structures were compatible with the ^1H NMR data (experimental section): 1,2,8-trihydroxyxanthone or 1,4,8-trihydroxyxanthone. The exclusion of the 1,2,8-pattern was based on the chemical shift of H-2 at d_H 6.70 (**1**), when compared with the corresponding H-3 (d_H 7.34) in the partial structure of 1,2,5-trihydroxyxanthone[9]. In addition, the C-H three bond correlation between the chelated hydrogen at d_H 11.05 (HO-1) and a carbon at d_C 110.51 (C-2), to which H-2 is attached (d_H 6.70, d, *J* 8.8 Hz, *ortho* coupling), excludes definitively the 1,2,8-pattern. The chemical shift of the hydrogen H-3 at d_H 7.37 (d, *J* 8.8 Hz, *ortho*-coupling constant) showed C-H long-range correlation (HMBC) with the carbons at d_C 154.21 [C-1, ^3J(CH)], 138.25 [C-4, ^2J(CH)] and 144.81 [C-4a, ^3J(CH)], revealing that the two hydroxyl groups were in positions 1 and 4. Furthermore, another hydroxyl hydrogen at d_H 11.83 (HO-8) was correlated with carbon signals at d_C 108.60 [C-8a, ^3J(CH)] and 111.47 [C-7, ^3J(CH)], the latter, bonded to H-7 (d_H 6.82, dd, *J* 8.4 and 0.8 Hz) that showed *ortho*-coupling with H-6 (d_H 7.76) and *meta*-coupling with H-5 (d_H 7.05). These data are in good agreement with those observed in the literature for an A-ring in the partial structure of euxanthone (**2**)[3,10-11]. These results established as **1** the structure of the new trioxygenated xanthone[1] (Figure 1).

Other xanthones were identified as 1,7-dihydroxyxanthone (euxanthone) (**2**)[3,10], 1,5-dihydroxy-8-methoxyxanthone (**3**)[2,3], 1,3,5,6-tetrahydroxyxanthone (**4**)[12] and 1,6-dihydroxy-7-methoxyxanthone (**5**)[13] by comparison with authentic samples (**2** and **3**), melting points and spectroscopic data in the literature.

Experimental

General procedures

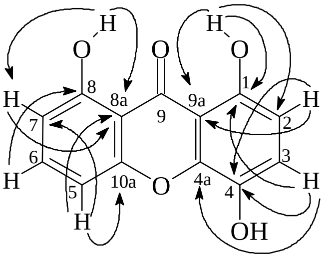
Melting points were obtained on a Mettler FP 80 HT. IR spectra were determined using a Shimadzu/IR - 408 spectrometer. ^1H and ^{13}C, NOESY, HMQC and HMBC spectra were recorded using a Bruker DRX-400 spectrometer.

Collection

Roots and stems of *Vismia latifolia* were collected in Bahia, Brazil in January 1996. A voucher specimen (register number 4580) is deposited at the Herbarium of the CEPLAC-CEPEQ (Centro de Pesquisas do Cacau - Ilhéus - Bahia)

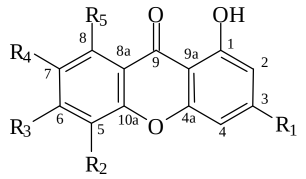
Extraction and fractionation of roots

The dried and ground roots (824 g) were extracted (at room temp.) with *n*-hexane (7.64 g) and EtOH (68.0 g) in succession. The ethanol extract was washed with ethyl ether and filtered. The soluble portion was evaporated under *vacuum* yielding 11.8 g of a residue that was chromatographed on silica gel (Merck) (220 g) CC and eluted with *n*-hexane-EtOAc, EtOAc-EtOH and EtOH. The twenty seven fractions obtained yielded six groups (A_1-A_6). A_5 (frs 12-17, 1.6 g) was rechromatographed on silica gel (30 g) CC using CH_2Cl_2-EtOAc, EtOAc-EtOH and EtOH as eluents. The twenty-four fractions obtained yielded five groups (A_{5a}-A_{5e}). From A_{5b} (frs 4-6) compound **1** (3.2 mg) was obtained as a yellow solid by recrystallization from $CHCl_3$ solution. A_{5c} (fr 7, 738 mg) was rechromatographed in silica gel (22 g) CC using *n*-hexane-CH_2Cl_2, CH_2Cl_2-EtOAc, EtOAc-EtOH and EtOH as eluents yielding forty-four fractions; from fr (21) compound **2** (3.0 mg) was isolated as a yellow solid by successive silica gel CC. A_{5d} (frs 12-



1

HMBC



	R_1	R_2	R_3	R_4	R_5
2	H	H	H	OH	H
3	H	OH	H	H	OCH_3
4	OH	OH	OH	H	H
5	H	H	OH	OCH_3	H

Figure 1. HMBC observed correlations of **1** and structural formulas of compounds **2**, **3**, **4** and **5**.

16) was washed with MeOH and the insoluble green solid obtained was rechromatographed successively on silica (Merck) flash-CC using *n*-hexane-acetone (3:2) as eluent yielding compound **3** (8.6 mg) as a yellow solid. A_6 (frs 18-25, 562 mg) was rechromatographed on silica gel (12 g) CC using *n*-hexane-EtOAc, EtOAc-EtOH and EtOH as eluent. The twenty-five fractions obtained yielded three groups (A_{6a}-A_{6c}). From A_{6b} (frs 13-17) compound **4** (2.0 mg) was obtained as a white amorphous solid by cellulose CC using EtOAc, EtOAc-EtOH and EtOH as eluent.

Extraction and fractionation of stems

Dried and ground stems (4.4 kg) were extracted (at room temp.) successively with *n*-hexane (17.35 g) and EtOH (50.0 g). The ethanol extract was chromatographed on silica gel (500 g) (Merck) CC and eluted with n-hexane-$CHCl_3$, $CHCl_3$-EtOAc, EtOAc-EtOH and EtOH. The one hundred fifty fractions obtained yielded twenty groups (B_1-B_{20}). Group B_7 (frs 26-31, 1.2 g) was rechromatographed on silica gel (24 g) CC using *n*-hexane-CH_2Cl_2, CH_2Cl_2-EtOAc, EtOAc-EtOH and EtOH as eluents; compound **5** (6.0 mg) was obtained as a pale yellow amorphous solid from frs (19-24) by washing with acetone.

1,4,8-Trihydroxyxanthone **1**

Yellow needles, mp 247-249 °C ($CHCl_3$). UV λ_{max}/nm (MeOH) (log ε): 205 (3.7), 235 (3.8), 255 (4.0), 270 (3.8), 340 (3.5); + NaOAc: 210 (4.5), 250 (3.9), 275 (3.6), 340 (3.5). IR $\nu_{Max.}$ (KBr)/cm^{-1} 3425, 3040, 1640, 1600, 1510, 1475. Positive EIMS (70 eV) *m/z* (rel. int.): 245 $[M+1]^+$ (18.2), 244 $[M]^+$ (100), 243 (9.4), 216 (2.5), 215 (2.4), 108 (5). ^1H NMR (400 MHz, acetone-d_6) *d* 6.70 (1H, d, *J* 8.8 Hz, H-2), 6.82 (dd, *J* 8.4, 0.8 Hz, H-7), 7.05 (dd, *J* 8.4, 0.8 Hz, H-5), 7.37 (d, *J* 8.8 Hz, H-3), 7.76 (t, *J* 8.4 Hz, H-6), 8.61 (s, HO-4), 11.05 (s, HO-1),11.83 (s, HO-8). ^{13}C NMR (100 MHz acetone-d_6) *d* 108.12 (CH-5), 111.47 (CH-7), 110.51 (CH-2), 138.25 (C-4), 108.60 (C-8a), 108.60 (C-9a), 154.21 (C-1), 125.51 (CH-3), 157.21 (C-10a), 162.35 (C-8), 144.81 (C-4a), 138.91 (CH-6), 187.53 (C9).

Acknowledgements

The authors thank Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento Pessoal de Ensino Superior (CAPES) for financial support and Dr. Rodinei Augusti (UFMG) for MS measurements.

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Received: July 14, 1999
Published on the web: September 15, 2000