Short Report

Xanthones from Vismia latifolia

Marcelo H. dos Santos\textsuperscript{a*}, Tanus J. Nagem\textsuperscript{b}, Marilda C. da Silva\textsuperscript{a} and Luiz G. F. e Silva\textsuperscript{a}

\textsuperscript{a}Departamento de Química, ICEx, Universidade Federal de Minas Gerais, Av. Antônio Carlos, 6627, Pampulha, 31270-901, Belo Horizonte, MG, Brazil.
\textsuperscript{b}Departamento de Química, Universidade Federal de Ouro Preto, 35400-000, Campus Morro do Cruzeiro, Ouro Preto, MG, Brazil.

Este trabalho relata o isolamento e a identificação de uma nova xantona, 1,4,8-triidroxixantona (1,4,8-triihdroxi-9\textsubscript{H}-xanthen-9-one), isolada das raízes de \textit{Vismia latifolia} (Guttiferae). Quatro outras xantonas conhecidas também foram isoladas: 1,5-diihydroxy-8-metoxixantona, 1,7-diihydroxyxantona, 1,6-diiidroxi-7-metoxixantona e 1,3,5,6-tetraidroxixantona, sendo as duas últimas inéditas no gênero \textit{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\textsubscript{H}-xanthen-9-one), was isolated from the roots of \textit{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 \textit{Vismia} species. The structures were established by UV, IR, MS, 1D and 2D NMR spectroscopic techniques.

**Keywords:** \textit{Vismia latifolia}, \textit{Guttiferae}, 1,4,8-trihydroxyxanthone, xanthones

Introduction

\textit{Vismia latifolia} Choisy (Syn. \textit{Hypericum latifolium} Aubl.), a tree known popularly in Bahia (Brazil) as "pau-de-sangue", is used as a tonic and febrifugal agent\textsuperscript{1}. This species belongs to the \textit{Guttiferae} family, subfamily \textit{Hypericoideae} and tribe \textit{Vismieae}. Previous papers have reported the presence of anthranoids, terpenoids, flavonoids and xanthones from \textit{Vismia} species\textsuperscript{2-6}. As part of a chemotaxonomic study of the \textit{Guttiferae} (\textit{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 \textit{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 \textit{Vismia} genus was described only in \textit{V. guaramirense}\textsuperscript{2} and \textit{V. parviflora}\textsuperscript{3}.

Results and Discussion

Purification of an ethanol extract of the roots of \textit{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\textsubscript{15}H\textsubscript{12}O\textsubscript{5} from its [M]\textsuperscript{+} 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\textsuperscript{-1} in the IR spectrum\textsuperscript{7}. The UV spectral data of 1 (experimental section) was characteristic of the xanthone chromophore\textsuperscript{8} and the sodium acetate addition caused a batochromic shift; the consecutive addition of H\textsubscript{3}BO\textsubscript{3} did not modify the UV spectrum, indicating the absence of the \textit{ortho} hydroxyls. The \textsuperscript{13}C NMR spectrum of 1 indicated the presence of signals corresponding to three aromatic hydrogens [\textdelta\textsubscript{C} 8.61 (s, HO-4), 11.05 (s, HO-1) and 11.83 (s, HO-8)] and two \textit{ortho}-coupled hydrogens [\textdelta\textsubscript{H} 6.70 (H-2) and 7.37 (H-3) (d, J 8.8 Hz)]. The \textsuperscript{13}C NMR spectrum of 1 showed 13 carbon signals: eight non hydrogenated carbons, including one carbonyl group (\textdelta\textsubscript{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

*e-mail: marcelo_hs@yahoo.com.br
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 $^1$H 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 $\delta_H$ 6.70 (1), when compared with the corresponding H-3 ($\delta_H$ 7.34) in the partial structure of 1,2,5-trihydroxyxanthone. In addition, the C-H three bond correlation between the chelated hydrogen at $\delta_H$ 11.05 (HO-1) and a carbon at $\delta$ 110.51 (C-2), to which H-2 is attached ($\delta_H$ 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 $\delta_H$ 7.37 (d, J 8.8 Hz, ortho-coupling constant) showed C-H long-range correlation (HMBC) with the carbons at $\delta_C$ 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 $\delta_H$ 11.83 (HO-1) was correlated with carbon signals at $\delta_C$ 108.60 [C-8a, $^3J(CH)$] and 111.47 [C-7, $^3J(CH)$], the latter, bonded to H-7 ($\delta_H$ 6.82, dd, $J$ 8.4 and 0.8 Hz) that showed ortho-coupling with H-6 ($\delta_H$ 7.76) and meta-coupling with H-5 ($\delta_H$ 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)$^{3,10,11}$, 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. $^1$H 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 five groups (A$_{1}$-A$_{6}$). A$_{5}$ (frs 12-17, 1.6 g) was rechromatographed on silica gel (30 g) CC using CH$_2$Cl$_2$-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 isolated as a yellow solid by recrystallization from CHCl$_3$ solution. A$_{5c}$ (fr 7, 738 mg) was rechromatographed on silica gel (22 g) CC using n-hexane-CH$_2$Cl$_2$, CH$_2$Cl$_2$-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-
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. A6 (frs 18-25, 562 mg) was rechromatographed successively on silica gel (12 g) CC using n-hexane-EtOAc, EtOAc-EtOH and EtOH as eluent. The twenty-five fractions obtained yielded three groups (A6a-A6c). From A6b (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-CHCl3, CHCl3-EtOAc, EtOAc-EtOH and EtOH. The one hundred fifty fractions obtained yielded twenty groups (B1-B20). Group B7 (frs 26-31, 1.2 g) was rechromatographed on silica gel (24 g) CC using n-hexane-CH2Cl2, CH2Cl2-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 (CHCl3). UV λmax/nm (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 νmax (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-d6) δ 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). 13C NMR (100 MHz acetone-d6) δ 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).

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