A new arylnaphthalene type lignan from *Cordia rufescens* A. DC. (Boraginaceae)

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Dedicated to Prof. Otto Richard Gottlieb

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Abstract
A new arylnaphthalene type lignan named rufescidride, the first containing an unusual anhydride moiety, has been isolated from the stem and branches of *Cordia rufescens*. Its structure was elucidated on the basis of spectral data (IR, MS and NMR), mainly 1D and 2D NMR.

Keywords: *Cordia rufescens*, Boraginaceae, arylnaphthalene lignan, rufescidride

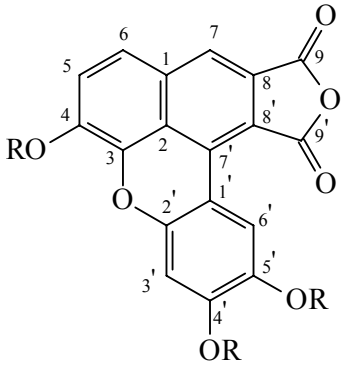
Introduction

The Boraginaceae family comprises about 130 genera and 2600 species distributed in temperate and tropical zones.[1] Terpenes, pyrrolizidine alkaloids, flavonoids and naphthoquinones have been frequently reported in this family. However, only 15 lignoids have been reported: lithospermic acid, lithospermic acid B, rabdosiin,[2] arnebia lignan caffeate 3, arnebia lignan caffeate 4, arnebia caffeate 5,[3] epi-rabdosiin,[4] iso-rabdosiin,[5] magnesium lithospermic acid,[6] buddlenol B, ehletianol C, ehletianol D, icariside E-5,[7] iso-salvianolic acid and salvianolic acid F.[8] Among all the lignoids above, only the magnesium salt of lithospermic acid was isolated from a species of the genus *Cordia*. *Cordia rufescens* A. DC. (Syn: *C. piauhiensis* Fresen) is a shrub popularly known in Northeastern Brazil as "ramela de velho". Some plants of the genus *Cordia* have been used in popular medicine as abortive,[9] anti-inflammatory,[10] and to treat dysmenorrhea and dyspepsia.[11] Only 3β-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl]

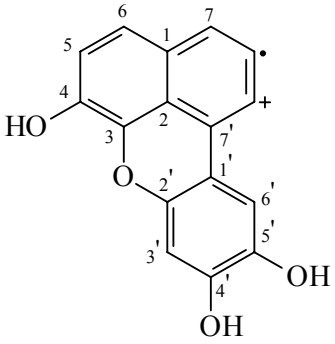
ursolic acid 28-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl] ester were reported from *C. rufescens*.[12] As a part of the study of the genus *Cordia* carried out by our group, this paper reports the isolation of a new arylnaphthalene type lignan, named rufescidride, from the stem and branches of *C. rufescens.*

Results and Discussion

The dried and ground stem and branches of *C. rufescens* were exhaustively extracted with EtOH at room temperature. The crude EtOH extract was fractionated with hexane, $CHCl_3$ and AcOEt. The chloroform fraction was subjected to column chromatography over silica gel yielding 3β-*O*-β-D-glucopyranosyl-β-sitosterol. The AcOEt fraction was subjected to successive chromatographic procedures on Sephadex LH-20 to yield the new arylnaphthalene lignan (1).



1 R=H
2 R=Ac



1a *m/z* 264

Figure 1. Rufescidride, rufescidride triacetate and the fragment attributed to the peak at m/z 264 observed in the EIMS.

The molecular formula $C_{18}H_8O_7$ for 1 was deduced by analysis of the EIMS, ^{1}H NMR and APT-^{13}C NMR spectra (Table 1). The presence of carbonyl functions belonging to the anhydride group was revealed by two absorptions at ν_{max} 1798 and 1737 cm $^{-1}$ observed in the IR spectrum, in agreement with the signals at δ_C 163.67 (correlated in the HMBC spectrum with the signal of H-7 at δ_H 8.14) and 163.38 in the ^{13}C NMR spectra (Table 1). This deduction was supported by the presence of the base peak at *m/z* 264, attributed to fragment 1a derived from the molecular ion at *m/z* 336 by loss of CO_2 + CO (C_2O_3 = 72). The ^{1}H NMR spectrum (200 MHz) of 1 (Table 1) showed the presence of three singlet signals at δ_H 8.81 (s, H-6′), 8.14 (s, H-7) and 6.73 (s, H-3′) and two doublets at δ_H 7.68 (d, *J*= 8.8 Hz, H-6) e 7.47 (d, *J*= 8.8 Hz, H-5). The existence of three hydroxyl groups was confirmed by ^{1}H NMR of its acetyl derivative 2, which reveled the presence of three acetyl signals at δ_H 2.44 (s, 3H), 2.35 (s, 3H) e 2.33 (s, 3H). Comparative analysis of the {^{1}H}- and APT-^{13}C NMR spectra (Table 1) showed eighteen signals: five for

methine aromatic carbons and thirteen for non-hydrogenated carbons [including five oxygenated: δ_C 138.55 (C-3), 143.79 (C-4), 151.58 (C-2′), 147.30 (C-4′) and 142.15 (C-5′)].

The 2D HMQC and HMBC spectra were also used to attribute the structure 1 and to complete ^{1}H and ^{13}C chemical shift assignments, summarized in Table 1. The cross correlations of C-1′ (δ_C 109.06) with H-3′ (δ_H 6.73, $^3J_{CH}$) and C-2′ (δ_C 151.58) with both H-3′ (δ_H 6.73, $^2J_{CH}$) and H-6′ (δ_H 8.81, $^3J_{CH}$) observed in the HMBC spectrum suggested the location of the hydrogens H-3′ and H-6′ in the same aromatic ring. Analogously way, the correlations between hydrogen H-7 (δ_H 8.14) and both carbon atoms C-2 (δ_C 110.82, $^3J_{CH}$) and C-9 (δ_C 163.67, $^3J_{CH}$) were used to locate the anhydride function. All the HMBC correlations are summarized in Figure 2.

The analysis of the spectral data (IR, MS and 1D and 2D NMR), comparison with literature values described for yunnaneic acid[13] and the significant deshielding revealed by the signals corresponding to H-5 ($\Delta\delta_H$ = 7.56 – 7.47 = 0.09), H-7 ($\Delta\delta_H$ = 8.24 – 8.14 = 0.10), H-3′ ($\Delta\delta_H$ = 7.22 – 6.73 = 0.49) and H-6′ ($\Delta\delta_H$ = 9.56 – 8.81 = 0.75) in the ^{1}H NMR spectrum of 2 established the structure 1, a new lignan of the arylnaphthalene type named rufescidride.

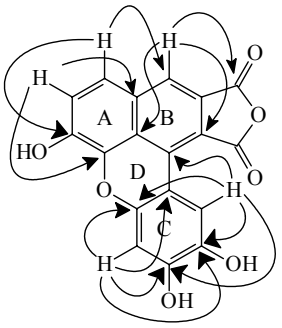


Figure 2. Heteronuclear correlations $^2J_{CH}$ and $^3J_{CH}$ (HMBC) for rufescidride.

Table 1. ^{1}H (200 MHz) and ^{13}C (50 MHz) NMR (1D and 2D) spectral data for compound **1**

		HMQC	HMBC	
C	δ_C	δ_H	$^2J_{CH}$	$^3J_{CH}$
1	128.03			H-5
2	110.82			H-7
3	138.55			H-5
4	143.79			H-6
5	121.08	7.47 (d, J = 8.8 Hz)		
6	122.83	7.68 (d, J = 8.8 Hz)		
7	124.38	8.14 (s)		H-6
8	123.77			
9	163.67			H-7
1′	109.06			H-3′

Table 1. Continued

2′	151.58		H-3′	H-6′
3′	103.06	6.73 (s)		
4′	147.30		H-3′	H-6′
5′	142.15		H-6′	H-3′
6′	114.82	8.81 (s)		H-6′
7′	133.35			H-7
8′	125.38			
9′	16338			

Experimental Section

General Procedures. IR spectra were recorded on a PERKIN-ELMER FT-IR. ^{1}H and ^{13}C NMR were measured on a MERCURY VARIAN spectrometer at 200 MHz using DMSO-D_6 (**1**) or $CDCl_3$ (**2**) as solvent and TMS as internal standard or by reference to the solvent signal (CD_2*H*SOCD_3 at δ_H 2.50 or C*H*Cl_3 at δ_H 7.24 and CD_3SOCD_3 at δ_C 39.5 or $CDCl_3$ and at δ_C 77.00). EIMS were obtained at 70 eV on a Shimadzu QP-2000 spectrometer.

Plant material. Stem and branches of *C. rufescens* were collected in August 2002 in the city Cruz do Espírito Santo, State of Paraíba, Brazil, A voucher specimen has been deposited at the Herbarium Prof. Lauro Pires Xavier (JPB) in the Universidade Federal da Paraíba.

Extraction and isolation. The stem and branches of *C. rufescens* (7000g), air-dried and powdered, were exhaustively extracted with EtOH at room temperature. The crude extract was taken up in MeOH:H_2O (7:3) and extracted successively with hexane, $CHCl_3$ and EtOAc (20 g). 10 g of the AcOEt fraction was subjected to column chromatography over Sephadex LH-20 using MeOH, resulting in 27 fractions. Fractions 6-8 (0,200 g) were reunited and subjected to successive CC over Sephadex LH-20 to yield compound 1 (0,017 g) as a red amorphous powder with melting point at 327-330 ^{o}C.

Acetyl derivative (**2**,: rufescidride triacetate)**.** Acetylation of **1** (Ac_2O, py) yielded **2** as a yellow amorphous powder (0,010 g) with melting point at 236-238 ^{o}C. δ_H ($CDCl_3$, 200 MHz) 2.33 (3H, s), 2.35 (3H, s), 2.44 (3H, s), 7.22 (1H, s), 7.56 (1H, d, *J*= 8.8 Hz), 7.68 (1H, d, *J*= 8.8 Hz,), 8.24 (1H, s), 9.56 (1H, s).

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