

## Trichotomol, a New Cadinenediol from *Cordia trichotoma*

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Um novo sesquiterpeno, nomeado trichotomol e compostos conhecidos como cordiachrome C,  $\alpha$ -cadinol, ácido oleanólico, oncalyxona A,  $\beta$ -sitosterol, glicosídeo do  $\beta$ -sitosterol, alantóina e sacarose foram isolados a partir do extrato etanólico do cerne de *Cordia trichotoma*. Suas estruturas foram determinadas por análises espectroscópicas e comparação com dados publicados para compostos estruturalmente relacionados.

A new sesquiterpene, named trichotomol, and known compounds cordiachrome C,  $\alpha$ -cadinol, oleanolic acid, oncalyxone A,  $\beta$ -sitosterol,  $\beta$ -sitosterol- $\beta$ -D-glucoside, allantoin and sucrose were isolated from the heart wood ethanol extract of *Cordia trichotoma*. Their structures were assigned unambiguously by spectroscopic analyses and comparison with the published data for structurally related compounds.

**Keywords:** *Cordia trichotoma*, Boraginaceae, sesquiterpene, trichotomol, cordiachrome C

### Introduction

*Cordia trichotoma* Vell. (Boraginaceae) is a tropical tree, popularly known as "frei jorge"<sup>1</sup>. According to a literature survey, several uses in traditional medicine such as cicatrizant, astringent, anti-inflammatory, antihelminthic, antimalarial, diuretic and to treat urinary infections, lung diseases and leprosy have been reported for several *Cordia* species<sup>2-4</sup>. No medicinal use has been reported for *C. trichotoma*, but its wood is recognized for its durability in carpentry and construction<sup>1</sup>. Previous phytochemical investigations of plants from this genus have described several natural products structurally related to terpenoid quinone and hydroquinones<sup>5-7</sup>. In the last few years, several articles have been published on this kind of compounds, from *Auxemma* genus<sup>8-10</sup>, belonging to the same family and formerly considered synonymous of *Cordia*. To the best of our knowledge, except for a publication in which the presence of eudesmol isomers from *C. trichotoma* wood<sup>11</sup> has been recorded, there have been no other reports of any similar chemical investigation in the literature. In this paper we describe the isolation and structure elucidation of the known compounds:  $\beta$ -sitosterol,

$\beta$ -sitosterol- $\beta$ -D-glucoside<sup>12</sup>, oleanolic acid<sup>13</sup>, allantoin<sup>14</sup>, sucrose<sup>15</sup>,  $\alpha$ -cadinol<sup>16</sup>, oncalyxone A<sup>8</sup>, cordiachrome C<sup>5</sup>, and a new sesquiterpene, trichotomol (**1**). Although cordiachrome C (**2**) had been previously isolated from *C. millenii*, only the partial <sup>1</sup>H NMR data was provided but some doubt about its stereochemistry<sup>5</sup> has remained. Here the complete <sup>1</sup>H and <sup>13</sup>C spectral data and assignments for **2** are reported for the first time and used to corroborate the stereochemical aspects.

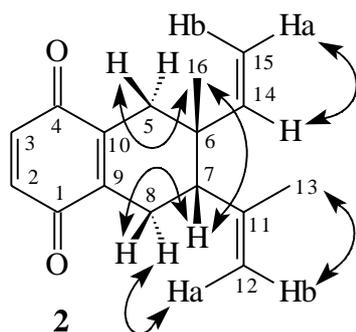
### Results and Discussion

Compound **1** was obtained as colorless crystals, mp 159-160 °C and  $[\alpha]_{589} = -17.1$  (*c* 0.7, CHCl<sub>3</sub>, 23 °C). Its IR spectrum revealed hydroxyl (3353 cm<sup>-1</sup> and 1116 cm<sup>-1</sup>) and olefinic (1657 cm<sup>-1</sup>) absorptions.

The molecular formula C<sub>15</sub>H<sub>26</sub>O<sub>2</sub>, which indicates three double-bond equivalents, was deduced using EIMS, <sup>13</sup>C NMR, and DEPT analyses. The <sup>13</sup>C NMR (BB and DEPT) spectra displayed signals corresponding to four methyl, four methylene, four methine, and three non-hydrogenated carbons. Resonances due to two olefinic carbons at  $\delta_C$  134.3 (C) and 124.7 (CH) in the <sup>13</sup>C NMR spectrum accounted for one double-bond equivalent,

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**Figure 2.**  $^1\text{H} - ^1\text{H}$  dipolar correlations of **2** observed through NOESY experiments.

## Experimental

### General experimental procedures

Melting points were determined using a melting point apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer 1000 FT-IR instrument. EIMS data were obtained using a VG-Auto Spec mass spectrometer. Optical rotations were measured in a Perkin-Elmer 341 digital polarimeter. The NMR spectra were recorded in a Bruker DRX 500 [500 MHz ( $^1\text{H}$ ) and 125 MHz ( $^{13}\text{C}$ )] spectrometer. Chemical shifts were recorded in  $\delta$  (ppm) from TMS relative to the solvent absorption relative to TMS,  $\text{CDCl}_3$   $\delta$  (7.24 and 77.0 ppm), and  $\text{DMSO}-d_6$  (2.49 and 39.5 ppm). Column chromatography (CC) was performed using silica gel 60 (Merck). TLC analysis were performed on precoated silica gel  $\text{UV}_{254}$  plates (Aldrich). Visualization of TLC plates was performed using a mixture of vanillin-perchloric acid-EtOH as a spray reagent. Spots were visualized by spraying the plates and then heating them at 100 °C for 1-3 min in an oven.

### Plant material

*Cordia trichotoma* was collected in March 1998, at the Meruoca mountain, State of Ceará, Brazil, and identified by A. S. Nogueira de Castro and E. P. Nunes, botanists of the Universidade Federal do Ceará, where a voucher specimen is deposited (Herbarium Prisco Bezerra, N $^{\circ}$ . 25.165).

### Extraction and Isolation

The air-dried and pulverized heartwood (2.0 kg) was exhaustively extracted with EtOH at room temperature and then concentrated under vacuum to yield 124.0 g of a brown residue. The ethanol extract was first fractionated by CC with hexane,  $\text{CHCl}_3$ , EtOAc and MeOH. The hexane fraction was subjected to CC and eluted with mixtures of hexane and EtOAc of increasing polarities to give  $\beta$ -sitosterol (176.0 mg, mp 162-164 °C), oleanolic acid (25.0 mg, mp

>300 °C),  $\alpha$ -cadinol (58.0 mg, mp 73-74 °C) and the new compound **1** (186.0 mg, mp 158-160 °C). Similarly, CC of the  $\text{CHCl}_3$  fraction, eluting with a hexane-EtOAc gradient, yielded oncocalyxone A (73.0 mg, mp 208-209 °C) and cordiachrome C (**2**, 32.6 mg). The EtOAc fraction gave  $\beta$ -sitosterol- $\beta$ -D-glucoside (287.0 mg, mp 289-292 °C), after repeated CC, using EtOAc-MeOH as eluent. From the MeOH fraction a precipitate was collected and was identified as sucrose (2.96 g, mp 185-186 °C). The residue from the supernatant MeOH fraction, after evaporation, was submitted to CC. Elution with increasing polarity with  $\text{CHCl}_3/\text{EtOAc}$  gave allantoin (630.0 mg, mp 230-232 °C).

**Compound 1.**  $\text{C}_{15}\text{H}_{26}\text{O}_2$ , 10 $\alpha$ ,11-dihydroxy-4-cadinene. (185.6 mg, 1.49 %); colorless crystal, mp 159 – 160 °C ( $\text{CHCl}_3$ );  $[\alpha]_{589} = -17.1$  (c 0.7,  $\text{CHCl}_3$ , 23 °C); IR  $\nu_{\text{max.}}/\text{cm}^{-1}$  3353, 2961, 2863, 1657, 1457, 1375, 1116 (KBr);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  1.26 (m, H-1), 1.99 (m, H-2 $\alpha$ ), 1.25 (m, H-2 $\beta$ ), 1.98 (m, H-3 $\beta$ ), 1.92 (m, H-3 $\alpha$ ), 6.14 (s, H-5), 1.93 (m, H-6), 1.21 (m, H-7), 1.75 (m, H-8 $\alpha$ ), 1.03 (m, H-8 $\beta$ ), 1.46 (dq,  $J$  3.4 and 12.5 Hz, H-9 $\alpha$ ), 1.78 (dq,  $J$  3.4 and 12.5 Hz, H-9 $\beta$ ), 1.19 (s, 3H-12), 1.20 (s, 3H-13), 1.09 (s, 3H-14), 1.64 (s, 3H-15);  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ , 500 MHz)  $\delta$  4.04 (s, HO-10), 4.11 (s, HO-11);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz),  $\delta$  49.8 (CH-1), 22.7 (CH $_2$ -2), 30.6 (CH $_2$ -3), 134.3 (C-4), 124.7 (CH-5), 40.8 (CH-6), 53.0 (CH-7), 27.1 (CH $_2$ -8), 42.3 (CH $_2$ -9), 72.1 (C-10), 74.2 (C-11), 24.1 (CH $_3$ -12), 32.1 (CH $_3$ -13), 20.7 (CH $_3$ -14), 24.1 (CH $_3$ -15); EIMS (70 eV)  $m/z$  220 (M – H $_2\text{O}$ , 5), 202 (M – 2H $_2\text{O}$ , 47), 43 (100).

**Compound 2.**  $\text{C}_{16}\text{H}_{18}\text{O}_2$ , 6-ethenyl-5,6,7,8-tetrahydro-6-methyl-7-(1-methylethenyl)-1,4-naphthalenedione. (32.6 mg, 0.026 %); orange oil;  $[\alpha]_{589} = -1.11$  (c 0.27,  $\text{CHCl}_3$ , 23 °C); IR  $\nu_{\text{max.}}/\text{cm}^{-1}$  2920, 2851, 1680, 1656, 1464, 1376, 1278, 908, 725 (film);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  6.69 (d,  $J$  9.2 Hz, H-2), 6.67 (d,  $J$  9.2 Hz, H-3), 2.66 (d,  $J$  19.4 Hz, H-5 $\alpha$ ), 2.24 (ddd,  $J$  19.4, 4.1 and 2.4 Hz, H-5 $\beta$ ), 2.18 (dd,  $J$  11.1 and 5.0 Hz, H-7), 2.60 (dd,  $J$  19.9 and 2.6 Hz, H-8 $\beta$ ), 2.44 (dddd,  $J$  19.9, 11.1, 4.1 and 2.0 Hz, H-8 $\alpha$ ), 4.89 (s, H-12a), 4.74 (s, H-12b), 1.73 (s, Me-13), 5.87 (dd,  $J$  17.5, and 10.9 Hz, H-14), 4.98 (d,  $J$  10.9 Hz, H-15a), 4.87 (d,  $J$  17.5 Hz, H-15b), 1.11 (s, Me-16);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  186.9 (C-1), 136.3 (CH-2), 136.3 (CH-3), 187.1 (C-4), 36.2 (CH $_2$ -5), 37.7 (C-6), 49.4 (CH-7), 26.5 (CH $_2$ -8), 141.6 (C-9), 140.7 (C-10), 145.0 (C-11), 113.8 (CH $_2$ -12), 23.1 (CH $_3$ -13), 141.3 (CH-14), 113.4 (CH $_2$ -15), 26.1 (CH $_3$ -16); EIMS (70 eV)  $m/z$  242 (M $^+$ , 15), 227 (M – CH $_3$ , 100), 199 (19).

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