POLYPRENOLS AND ACYLPHLOROGLUCINOLS FROM

ESENBECKIA NESIOTICA*

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INTRODUCTION

The occurrence of flavonoids, lignans, coumarins, alkaloids and limonoids in the Rutaceae has been established [1]. In particular, the three last types of compound are considered as the main constituents of Esenbeckia [2–5], a genus comprising ca 30 species [6]. In connection with our chemical investigation of Mexican plants [7], herein we report the chemical constituents of Esenbeckia nesiotica.

RESULTS AND DISCUSSION

A hexane-soluble fraction of the leaves of E. nesiotica was chromatographed on silica gel to give β-sitosterol, caryophyllene β-oxide, friedelin, a mixture of polyrenols, lupeol, clovandiol and a mixture of phloroglucinols. These compounds were biosynthesized by Esenbeckia nesiotica; 3-geranyl-1(3-methylbutanoyl)-phloroglucinol is a new natural product. This is the first report of the occurrence of polyrenols in the Rutaceae. Polyrenols did not display toxicity in the Artemia salina bioassay but the phloroglucinols showed moderate activity. Was UV absorptions at 223 and 290 nm indicated the presence of a benzenoid ring. 1H NMR data (Table I) of the mixture (3a–5a) showed the presence of a geranyl residue. Treatment with Ac2O and pyridine afforded initially a mixture of diacetylated phenols 3b, 4b and 5b, which finally gave triacetylated phenols 3c, 4c and 5c, establishing that the natural products were phloroglucinol derivatives acylated with different acyl residues. Careful analysis of the 2D 1H NMR spectrum of the phloroglucinol mixture established the presence of the acyl fragments. The 3-methylbutanoyl residue of 3a was characterized by the methine heptuplet at δ2.26 (H-3') and 60.97 (H-4' and H-5'). Analogous correlations indicated the presence of 2-methylbutanoyl and 2-methylpropanoyl residues in 4a and 5a, respectively. The area under the H-2' signal of each compound established a 3:3:1 ratio of 3a, 4a and 5a in the mixture. The structures 3a–5a were in agreement with (a) the upfield shifts of H-7 and H-8 and the downfield shift of H-5 observed in the diacetyl and triacetyl derivatives 3b–5b and 3c–5c, respectively (Table I), and (b) the mass spectral fragmentation pattern of the mixture (Scheme I), in particular, the presence of the fragments m/z 346 [M]+, 277, 223 for 3a and 4a, and the fragments m/z 332 [M]+, 263, 209 for 5a. 13C NMR of the mixture of 3a–5a confirmed the structures and are reported in the Experimental. The assignments were made by comparative analysis with published data [31, 32]. 3-Geranyl-1(3-methylbutanoyl)-phloroglucinol (3a) represents a new natural product, but 4a and 5a have been previously reported [32]. The mixture (3a–5a) displayed toxicity in the brine shrimp bioassay [29] (LC50 = 307 ppm). The occurrence of acylphloroglucinols in Esenbeckia is unprecedented, although this type of compound has been reported from other Rutaceae [31].

EXPERIMENTAL

Plant material. Leaves of E. nesiotica Stand. were collected in the Hwy Playa Azul to Tecomán, State of Michoacán, México.

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A voucher specimen is deposited at the National Herbarium, Instituto de Biologia [UNAM (MEXU, CHR-84)].

**Extraction and isolation.** Air-dried plant material (1.9 kg) was extracted with n-hexane at room temp. (×2) affording 37 g of residue. The defatted plant material was then extracted with Me$_2$CO to obtain 108 g of residues. The crude hexane extract was adsorbed on to silica gel and carefully chromatographed on a column of silica gel via vacuum CC (VLC) [33] eluting with n-hexane and n-hexane containing increasing proportions of EtOAc. This procedure allowed the isolation of friedelin (204 mg), caryophyllene β-oxide (117 mg), a mixt. of polyprenols (1.2 g), lupeol (148 mg) and p-sitosterol (190 mg).

The polyprenyl fr. was subjected to repeated CC on silica gel using hexane. Two sets of frs were subjected to repeated HPLC analysis using a Hypersil ODS reverse-phase column, using n-PrOH. This procedure allowed the isolation of [3E,6Z]-13-prenol (1.40 mg) [11] and [3E,6Z]-10-prenol (2.25 mg) [12] as oils. Compound 1: UV $\lambda_{max}$ nm (log ε): 197 (5.06). IR $\nu$ cm$^{-1}$: 3330, 2960, 2920, 2850, 1665, 1445, 1378, 1000, 830. $^1$H NMR (300 MHz, CDCl$_3$): 5.12 (1H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 2.03 (48H, br s, $-\text{CH}_2\text{-CH}_2$), 1.75 (3H, s, $-\text{Me}$), 1.58 (12H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.58 (12H, s, $-\text{Me}$), 1.58 (12H, s, $-\text{Me}$).

Compound 2: $^1$H NMR (300 MHz, CDCl$_3$): 3.73 (1H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 2.01 (36H, br s, $-\text{CH}_2\text{-CH}_2$), 1.75 (3H, s, $-\text{Me}$), 1.58 (12H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.58 (12H, s, $-\text{Me}$), 1.58 (12H, s, $-\text{Me}$).

Compound 3: $^1$H NMR (300 MHz, CDCl$_3$): 3.73 (1H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 2.01 (36H, br s, $-\text{CH}_2\text{-CH}_2$), 1.75 (3H, s, $-\text{Me}$), 1.58 (12H, $d$, $J = 7$ Hz, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.67 (27H, s, $-\text{CH}_2\text{-OH}$), 1.58 (12H, s, $-\text{Me}$), 1.58 (12H, s, $-\text{Me}$).

**Scheme 1.** Mass spectral fragmentation pattern of compounds 3a–5a.
Constituents of *Esenbeckia nesiotica* 3493

26.6 (t, C-4 trans), 26.5, 26.4, 26.3, 26.2 (t, C-4 cis), 25.7 (q, C-5-5trans), 23.4 (q, C-5 cis), 23.3 (q, C-5=5a), 17.7 (q, C-5=5o), 16.0 (q, C-5 trans).

The MeCO extract was adsorbed on to silica gel and chromatographed on silica gel using VLC [33] and n-hexane–EtOAc (20:1). Increasing proportions of EtOAc were used for elution. This procedure allowed the isolation of 2 g of residue which was further chromatographed to afford 1.6 g of a mixt. of 3a, 4a, 5a in a ratio of 3:3:1. Mp 128-130°. UV 

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\text{\textit{\textit{nm}} (\log E)}: 207 (4.45) 223 (4.27), 290 (4.35).
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IR \(\text{\textit{cm}^{-1}}\): 3570, 3360, 2960, 2920, 2870, 1630, 1610, 1430, 1365, 1060.

\[\text{\textit{H NMR}} (300 \text{ MHz, CDCl}_{3}) \text{ in Table 1.} \]

\[\text{\textit{13C NMR}} (75 \text{ MHz, CDCl}_{3}) \text{ in Table 1.}\]

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