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BUTANOLIDES AND A NEOLIGNAN FROM THE FRUITS OF *IRYANTHERA PARAENSIS* HUBER*

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Key Word Index—*Iryanthera paraensis*; Myristicaceae; fruits; benzodioxane neolignans; arylalkyl butanolides.

Abstract—Five new compounds were isolated from fruits of *Iryanthera paraensis*: (2*S*, 3*R*)-5-methoxy-3-methyl-2-(4-hydroxy-3-methoxy-phenyl)-7-propenyl-2,3-dihydro-benzo[1,4]dioxane, (2*S*, 3*S*, 4*S*)-2-(9′-phenyl-*n*-nonyl)-3-hydroxy-4-methyl-butanolide; (2*S*, 3*R*, 4*S*)-2-(9′-phenyl-*n*-nonyl)-3-hydroxy-4-methyl-butanolide; (2*S*, 3*S*, 4*S*)-2-(11′-phenyl-*n*-undecyl)-3-hydroxy-4-methyl-butanolide; and (2*S*, 3*R*, 4*S*)-2-(11′-phenyl-*n*-undecyl)-3-hydroxy-4-methyl-butanolide.

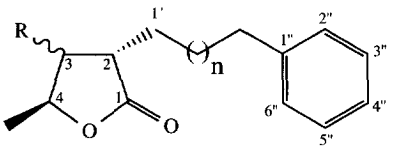
INTRODUCTION

Previous studies carried out on *Iryanthera* species revealed the occurrence of butanolides such as juruenolide [1] and grandinolide [2], besides lignoflavonoids and tocotrienols [3, 4]. This paper deals with phytochemical investigations on unripe fruits of *I. paraensis* collected near Belém, Brazil. Four new arylalkyl butanolides (**1a**, **1b**, **2a**, and **2b**) and a new benzodioxane neolignan (**3**) have been isolated as major components from the chloroform extract of the fruits.

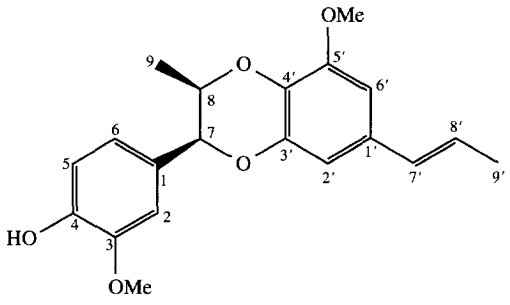
Nomenclature and numbering of the neolignan in the text follows the rules outlined in the literature [5].

RESULTS AND DISCUSSION

Compounds **1a**, **1b**, **2a** and **2b** were recognized as γ-lactones by IR carbonyl absorptions at 1750±3 cm^{-1}. The multiplets at δ 1.27 and δ 7.22 in their ^1H NMR spectra and the ion at *m/z* 91 indicated the presence of alkylphenyl groups in these compounds. The absorptions at δ 1.4 and δ 1.34 for **1a/2a** and **1b/2b** respectively and a multiplet at δ 4.2 for these compounds, associated to intense peaks at *m/z* 116 and 129 in the mass spectrum, indicated one hydroxyl and methyl groups bearing the lactone ring. Considering the absence of other functional groups in these molecules and the difference of 28 unities for molecular ion in their mass spectra, $n = 7$ and $n = 9$ can be deduced for **1** and **2**, respectively. The pairs **1a/2a** and **1b/2b** showed distinct chemical shifts for Me-4 (δ 13.8 vs δ 18.1, respectively) and C-1′ (δ 27.2 vs δ 23.2, respectively) in their ^{13}C NMR spectra. These differences can be explained by γ-protection for the β-methyl group at C-4 by β-hydroxyl group at C-3 in **1a/2a**, and the same range of protection for the methylene group at C-1′ by α-hydroxyl group at C-3 in **1b/2b**. These data is in accordance with previously described structure



1a n=7 R=β-OH
1b n=7 R=α-OH
2a n=9 R=β-OH
2b n=9 R=α-OH



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elucidation based on Eu(fod)$_3$ induced ^{1}H NMR chemical shifts [2]. The most prominent result from NOE experiments carried out on **1a** was the increase for H-3 signal on irradiation at the H-4 frequency, which is in accordance with the proposed configurations. With the β-configuration for hydroxyl groups, negative optical rotations were observed for **1a/2a**, while in their epimers **1b/2b**, positive optical rotations were observed, in agreement with the signals for model compounds [1, 2].

Compound **3** showed characteristic chemical shifts of a benzodioxane neolignan judging by the absorptions at δ 4.83 (*d*, 3.2 Hz, H-7), δ 4.35 (*dq*, 6.3, 3.2 Hz, H-8), and δ 1.16 (*d*, 6.3 Hz, H-9) and δ 82.2 (C-7), δ 73.8 (C-8) and δ 13.4 (C-9) observed in its ^{1}H NMR and ^{13}C NMR spectra. The differences in the spectrum of **3** to that of the previously described eusiderin D [6] are due to propenyl and 4-hydroxy-3-methoxyphenyl groups in **3** instead of allyl and veratryl groups. The *cis*-arrangement of the methyl and aryl groups on the benzodioxane ring is evidenced by absorption of Me-9 (δ 1.16 and δ 13.4, respectively in their ^{1}H and ^{13}C NMR spectra) and $J_{H7,H8}$ (3.2 Hz) [6]. The NOE experiments showed that H-7 must be beyond the non-bonded interaction range of the neighbouring H-8 substituent by an increase in the H-8 signal after irradiation at the H-7 frequency.

The 7*S*,8*R* configuration for **3** was established by comparison with CD extremes of eusiderin J [7].

The occurrence of diastereoisomeric γ-lactones has not been detected yet in the same species of *Iryanthera*. The γ-lactones previously isolated from *Iryanthera* species have methylene chains with $n = 17$ and $n = 19$, while in this case the length ($n = 5$) is comparable to a γ-lactone isolated from seedlings leaves of *Virola surinamensis* [8].

EXPERIMENTAL

Isolation of constituents. Unripe fruits of *I. paraensis* were collected at Mocambu Reserve, Belém, Pará State during July 1989. The pericarps (57 g) were removed from the fruits, and were dried, ground and exhaustively extracted with chloroform. The extract (3.2 g) was chromatographed on Si gel (62 g), eluting with solvents of increasing polarity (C_6H_{14}, CH_2Cl_2, and EtOAc) to give 15 pooled frs. F-9 (1.5 g) was rechromatographed on Si gel CC (50 g) eluting with C_6H_{14}–EtOAc gradient. The following frs were eluted with the indicated solvents, to afford: F-9.3 (175 mg) (C_6H_{14}–EtOAc, 8:2); F-9.6 (59 mg) (C_6H_{14}–EtOAc, 18:7). F-9.3, submitted to HPLC (RP-18, 250 × 22 mm, MeOH–H_2O, 60–75% of MeOH in 60 min) gave a mixture of **1a/1b** and **2a/2b**, which submitted to HPLC (Si-10 μm, 250 × 4.6 mm, C_6H_{14}–EtOAc, 4:1), gave **1a** (28 mg), **1b** (9 mg), and **2a** (6 mg), **2b** (5 mg). F-9.6 was submitted to HPLC (RP-8, 250 × 22 mm, MeOH–H_2O, 6:4) yielding **3** (30 mg).

(2S,3S,4S)-2-(9′-Phenyl-n-*nonyl*)-3-*hydroxy*-4-*methyl-butanolide* (**1a**). Mp 67° ($CHCl_3$), $[\alpha]_D^{25}$ −3.5° (MeOH, *c* 0.22). Analyt. Calcd for $C_{20}H_{30}O_3$: C-75.5, H-9.4, O-15.1. Found: C-75.4, H-9.7, O-14.8. EI-MS *m/z* (rel. int.): 318 $[M]^+$ (100), 300 (8), 273 (11), 227 (13), 202 (3), 189 (1), 161 (2), 157 (3), 129 (39), 104 (32), 92 (20), 91 (59), 71 (16), 69 (16), 57 (30), 55 (20). IR ν_{max}^{film} cm^{-1}: 3436, 2928, 2855, 1752, 1455, 1341, 1190, 1138, 1055, 996, 700. ^{1}H NMR (δ, 200 MHz, $CDCl_3$): 2.44–2.54 (*m*, H-2), 4.17 (*dd*, *J* = 7.8, 4.9 Hz, H-3), 4.61 (*dq*, *J* = 6.5, 4.9 Hz, H-4), 1.39 (*d*, *J* = 6.5 Hz, Me-4), 2.60 (*t*, *J* = 7.8 Hz, H_2C-Ar), 7.13–7.31 (*m*, C_6H_5), 1.28 [*br s*, $(H_2C)_n$]. ^{13}C NMR (δ, 50 MHz, $CDCl_3$): 178.0 (C-1), 49.2 (C-2), 73.9 (C-3), 78.4 (C-4), 13.8 (Me-4), 27.2 (C-1′), 28.4 (C-2′), 29.3 (C-3′, C-4′, C-5′), 29.4 (C-6′, C-7′), 31.4 (C-8′), 35.9 (C-9′), 142.8 (C-1″), 128.3 (C-2″, C-6″), 128.2 (C-3″, C-5″), 125.5 (C-4″).

(2S,3R,4S)-2-(9′-*Phenyl*-n-*nonyl*)-3-*hydroxy*-4-*methyl-butanolide* (**1b**). Mp 35° (MeOH), $[\alpha]_D^{25}$ +2.0° (MeOH, *c* 0.16). Analyt. Calcd for $C_{20}H_{30}O_3$: C-75.5, H-9.4, O-15.1. Found: C-75.3, H-9.6, O-14.9. EI-MS *m/z* (rel. int.): 318 $[M]^+$ (53), 300 (2), 273 (9), 227 (10), 202 (2), 157 (2), 129 (75), 117 (19), 116 (62), 104 (41), 99 (21), 92 (39), 91 (100), 85 (7), 71 (6), 69 (10), 57 (23). IR ν_{max}^{film} cm^{-1}: 3435, 2979, 2927, 2854, 1752, 1455, 1364, 1181, 1103, 1030, 699. ^{1}H NMR (δ, 200 MHz, $CDCl_3$): 2.55–2.57 (*m*, H-2), 4.17 (*t*, *J* = 4.5 Hz, H-3), 4.50 (*q*, *J* = 6.8 Hz, H-4), 1.34 (*d*, *J* = 6.8 Hz, Me-4), 2.55 (*t*, *J* = 8.0 Hz, H_2C-Ar), 7.16–7.27 (*m*, C_6H_5), 1.27 [*br s*, $(H_2C)_n$]. ^{13}C NMR (δ, 50 MHz, $CDCl_3$): 177.3 (C-1), 43.7 (C-2), 73.8 (C-3), 82.4 (C-4), 18.1 (Me-4), 23.3 (C-1′), 27.6 (C-2′), 29.3 (C-3′), 29.4 (C-4′, C-5′, C-6′), 29.5 (C-7′), 31.5 (C-8′), 35.9 (C-9′), 142.9 (C-1″), 128.4 (C-2″, C-6″), 128.2 (C-3″, C-5″), 125.5 (C-4″).

(2S,3S,4S)-2-(11′-*Phenyl*-n-*undecyl*)-3-*hydroxy*-4-*methyl-butanolide* (**2a**). Mp 44° ($CHCl_3$), $[\alpha]_D^{25}$ −5.0° (MeOH, *c* 0.06). Analyt. Calcd for $C_{22}H_{34}O_3$: C-76.3, H-9.8, O-13.9. Found: C-76.0, H-9.9, O-14.0. EI-MS *m/z* (rel. int.): 346 $[M]^+$ (66), 230 (3), 255 (11), 217 (1), 161 (3), 129 (73), 116 (100), 104 (52), 99 (32), 92 (38), 91 (92), 85 (23), 71 (24), 69 (27), 57 (61), 55 (37). IR ν_{max}^{film} cm^{-1}: 3516, 2925, 1746, 1466, 1454, 1234, 1197, 1061, 994, 936. ^{1}H NMR (δ, 200 MHz, $CDCl_3$): 2.49–2.53 (*m*, H-2), 4.18 (*dd*, *J* = 7.8, 4.9 Hz, H-3), 4.62 (*dq*, *J* = 6.5, 4.9 Hz, H-4), 1.40 (*d*, *J* = 6.5 Hz, Me-4), 2.60 (*t*, *J* = 7.8 Hz, H_2C-Ar), 7.16–7.31 (*m*, C_6H_5), 1.26 [*br s*, $(H_2C)_n$]. ^{13}C NMR (δ, 50 MHz, $CDCl_3$): 177.5 (C-1), 49.3 (C-2), 74.1 (C-3), 78.1 (C-4), 13.9 (Me-4), 27.2 (C-1′), 28.4 (C-2′), 29.3 (C-3′, C-4′, C-5′), 29.4 (C-6′, C-7′, C-8′, C-9′), 31.5 (C-10′), 35.9 (C-11′), 143.0 (C-1″), 128.2 (C-2″, C-6″), 128.4 (C-3″, C-5″), 125.5 (C-4″).

(2S,3R,4S)-2-(11′-*Phenyl*-n-*undecyl*)-3-*hydroxy*-4-*methyl-butanolide* (**2b**). Mp 39° (MeOH), $[\alpha]_D^{25}$ +1.6° (MeOH, *c* 0.06). Analyt. Calcd for $C_{22}H_{34}O_3$: C-76.3, H-9.8, O-13.9. Found: C-76.1, H-10.0, O-13.8. EIMS *m/z* (rel. int.): 346 $[M]^+$ (100), 255 (23), 230 (4), 217 (2), 157 (4), 129 (73), 116 (70), 104 (41), 99 (20), 92 (34), 91 (83), 85 (12), 71 (14), 69 (16), 57 (32), 55 (24). IR ν_{max}^{film} cm^{-1}: 3441, 3026, 2926, 2854, 1752, 1455, 1383, 1104, 1059, 1031. ^{1}H NMR (δ, 200 MHz, $CDCl_3$): 2.56–2.58 (*m*, H-2), 4.19 (*t*, *J* =

4.5 Hz, H-3), 4.50 (*q*, $J = 6.8$ Hz, H-4), 1.34 (*d*, $J = 6.8$ Hz, Me-4), 2.63 (*t*, $J = 7.2$ Hz, H_2C-Ar), 7.14–7.31 (*m*, C_6H_5), 1.27 [*br s*, $(H_2C)_n$]. ^{13}C NMR (δ, 50 MHz, $CDCl_3$): 177.2 (C-1), 43.7 (C-2), 74.0 (C-3), 82.4 (C-4), 18.1 (Me-4), 23.4 (C-1′), 27.7 (C-2′), 28.4 (C-3′), 29.3 (C-4′, C-5′), 29.4 (C-6′, C-7′), 29.5 (C-8′, C-9′), 31.5 (C-10′), 36.0 (C-11′), 142.9 (C-1″), 128.4 (C-2″, C-6″), 128.2 (C-3″, C-5″), 125.5 (C-4″).

(7S,8R) - 4 - *Hydroxy* - 3,5′ - *dimethoxy*-Δ:1,3,5,1′,3′,5′,7′-7.O.3′,8.O.4′-*neolignan* (**3**). Viscous oil, $[\alpha]_D^{25}$ −8.0° ($CHCl_3$, *c* 0.2). Analyt. Calcd for $C_{20}H_{22}O_5$: C-70.1, H-6.4, O-23.4. Found: C-69.8, H-6.6, O-23.7. EI-MS *m/z* (rel. int.): 342 $[M]^+$ (10), 208 (10), 207 (6), 191 (10), 181 (20), 180 (40), 178 (4), 165 (25), 164 (100), 163 (16), 153 (62), 137 (48), 135 (10), 93 (23), 91 (28), 77 (25), 65 (22). CD (MeOH; *c* 4.0 mg per 25 ml): $[\theta]_{225}$ −4807, $[\theta]_{251}$ O, $[\theta]_{275}$ +4800. IR ν_{max}^{film} cm^{-1}: 3435, 2927, 2854, 1747, 1641, 1188, 747, 699, 665, 541, 471. ^1H NMR (δ, 80 MHz, $CDCl_3$): 4.83 (*d*, $J = 3.2$ Hz, H-7), 4.35 (*dq*, $J = 6.3$, 3.2 Hz, H-8), 1.16 (*d*, $J = 6.3$ Hz, Me-9), 3.87 (*s*, MeO-3 and 5′), 5.62 (*br s*, HO-4), 1.87 (*d*, $J = 5.0$ Hz, Me-9′), 6.10 (*dq*, $J = 5.0$, 15.7 Hz, H-8′), 6.39 (*d*, $J = 15.7$ Hz, H-7′), 6.68–6.97 (*m*, H-2, H-5, H-6, H-2′, H-6′). ^{13}C NMR (δ, 50 MHz, $CDCl_3$): 124.7 (C-1), 114.0 (C-2), 146.5 (C-3), 144.9 (C-4), 119.2 (C-5), 119.0 (C-6), 82.2 (C-7), 73.8 (C-8), 13.4 (C-9), 133.6 (C-1′), 109.1 (C-2′), 151.5 (C-3′), 132.0 (C-4′), 145.8 (C-5′), 109.6 (C-6′), 130.5 (C-7′), 119.6 (C-8′), 18.3 (C-9′), 55.8 (MeO-5), 55.1 (MeO-5′).

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