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FLAVONOLIGNOID FROM THE FRUIT OF *IRYANTHERA LAEVIS*[*]

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Key Word Index—*Iryanthera laevis*; Myristicaceae; dihydrochalcones; flavonolignoid.

Abstract—The fruit of *Iryanthera laevis* was found to contain dihydrochalcones, including the novel 2′,4′,6′-trihydroxy-4-methoxy- and 3′-(7″-allylphenyl)-2′,4′,4″-trihydroxy-4,6′-dimethoxy-derivatives. The structures of aryltetralin type neolignans from *Virola calophylloidea*, another Colombian species of the Myristicaceae, is revised with respect to the position of a methoxyl which is located at C-6 and not at C-5 as originally proposed.

INTRODUCTION

Iryanthera laevis Markgr. is a myristicaceous tree called 'mamita' in the Oriental Llanos of Colombia. Its ripe fruit is used in the preparation of a sweet for consumption by the local population and its chemical analysis was thus deemed to be of importance. A previous study [2] on the woody part of the plant reported the presence of the dihydrochalcone **1a**. The present study shows **1a** to occur also in the fruit where it is accompanied by at least two additional new dihydrochalcones (**1b**, **2a**).

RESULTS

The dihydrochalcone **1a** was identified by direct comparison with an authentic sample. The structure is consistent with ^{1}H and ^{13}C NMR spectra, the latter reported only partly in the original description of the compound [2]. Comparison of these spectra with the analogous spectra obtained for **1b** indicated this new flavonoid to be simply a de-*O*-methyl-**1a**. The MS of both, **1a** and **1b**, show intense peaks assigned to ions **3** and **4**, but are, as hence was to be expected, differentiated by peaks assigned respectively to ions **5a** and **5b**.

A combination of NMR ^{1}H and ^{13}C counts with MS led to the molecular formulas $C_{17}H_{18}O_5$ for **1a** and to $C_{26}H_{26}O_6$ for **2a**. With one exception all NMR signals of **1a** are also present in the analogous spectra of **2a**, which thus must also be at least partly a dihydrochalcone. Again as in **1a**, NMR evidence concerning the phloroglucinol type ring A shows only one of the hydroxyls in **2a** to be vicinal to the carbonyl (^{1}H δ14.55). The additional *ortho*-position must hence carry a methoxyl. The exception refers to the signals due to ring A [^{1}H δ5.97, 6.04, two *d*, *J* = 2 Hz (**1a**) *vs* δ6.17, *s* (**2a**); ^{13}C δ97.0 (**1a**) *vs* 114.8 (**2a**)]. Position 3′ of **2a** must carry the substituent C_9H_9O ($C_{26}H_{26}O_6$ minus $C_{17}H_{17}O_5$). The alternative position 5′ is a less likely candidate in view of the differential UV behaviour upon addition of aluminium chloride, a bathochromic shift of maxima (**1a**) vs no spectral modification and hence steric hindrance to aluminium-chelate formation (**2a**). Furthermore the sole unsubstituted aromatic position on ring A of **2a** is represented by a ^{13}C-doublet at δ91.8, comparable with the doublet at δ92.1 of the model compound **6a** and not with the doublet at δ100.6 of the model compound **6b**. [3]. Lastly both methoxyls of **2a** must be vicinal at least to one unsubstituted position (^{13}C δ55.4, 55.9). The substitution of both *ortho*-positions is expected to cause a signal around 63.5 [3].

The C_9 substituent was easily recognized as shown in **2a** by comparison of the pertinent ^{1}H NMR signals with the analogous signals corresponding to the lignoid $C_6 \cdot C_3$-unit of neoflavonoids [4]. Confirmation was forthcoming through the NMR study of dihydro-**2a**. This identifies clearly an ethyl group (^{1}H δ0.83, *t*; 1.95–2.45, *m*. ^{13}C δ13.4, *q*; 25.6, *t*), a 4-hydroxyphenyl (δ7.15 AA′, 6.78 BB′, *J ca* 8.5 Hz) and, most importantly, a doubly benzylic proton (^{1}H δ4.40, *t*, *J* = 8 Hz. ^{13}C δ41.5, *d*).

DISCUSSION

The structure of **2a** implies not only in the cinnamoylation of a triacetate unit, a fundamental reaction leading via chalcones to flavonoids (including dihydrochalcones), but also in the cinnamylation of such a unit. The rationale for the introduction of a benzylic methine may be the enhancement of the biological activity of the parent flavonoid via oxidation to quinone methide forms. This was proposed to occur with neoflavonoids of Fabaceae and synthetic analogues [5]. In angiosperms such an enhancement is usually promoted by prenylation of phenols, a reaction which, albeit common in the rosiflorean block, is extremely rare in the families of the magnolialean block [6]. Here benzylic hydrogens are introduced via benzylation in the Annonaceae and, as suggested by the present finding, via cinnamylation in the related Myristicaceae.

The previous paper in this series on the chemistry of Colombian Myristicaceae reported the isolation from

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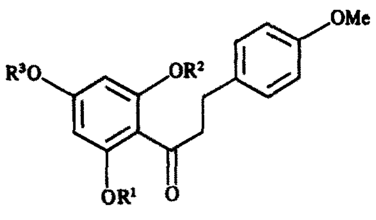
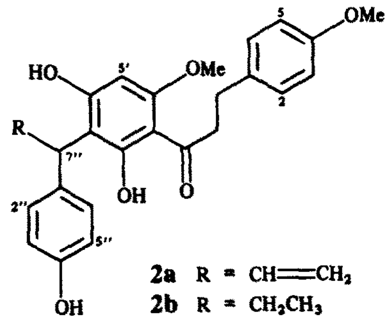
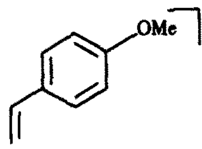
[*] Part 5 in the series 'The Chemistry of Colombian Myristicaceae'. For part 4 see ref. [1]. Taken in part from the undergraduate thesis presented by L. G. N. to Universidad Nacional de Colombia (1985).



1a R¹ = R³ = H, R² = Me
1b R¹ = R² = R³ = H
1c R¹ = R² = R³ = Ac



2a R = CH=CH₂
2b R = CH₂CH₃



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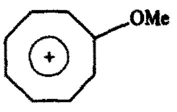

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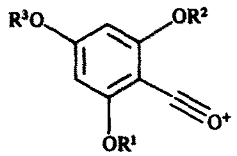
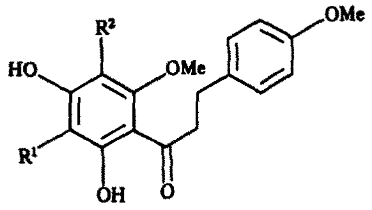
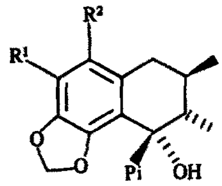


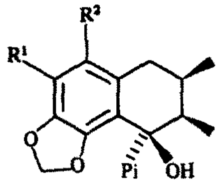
5a R¹ = R³ = H, R² = Me
5b R¹ = R² = R³ = H



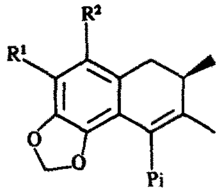
6a R¹ = *ortho*-hydroxybenzyl, R² = H
6b R¹ = H, R² = *ortho*-hydroxybenzyl



7a R¹ = OMe, R² = H
7b R¹ = H, R² = OMe
7c R¹ = R² = H



8a R¹ = OMe, R² = H
8b R¹ = H, R² = OMe



9a R¹ = OMe, R² = H
9b R¹ = H, R² = OMe

Pi = piperonyl

Virola calophylloidea of two aryltetralin type neolignans and of a dehydrated derivative. The proposed respective structures **7a**, **8a** and **9a** for these compounds [1] must be revised to **7b**, **8b** and **9b**. Experimental ^{13}C NMR data (C-1 to C-6, δ118.6, 126.4, 142.2, 145.5, 93.6, 150.9) were consistent with calculated data [7] for the additional presence on **7c** [8] of a methoxyl at C-6 (C-1–C-6, δ131.0–14.4 = 116.6, 126.1 + 1.0 = 127.1, 144.9–7.7 = 137.2, 145.6 + 1.0 = 146.6, 108.0–14.4 = 93.6, 120.7 + 31.4 = 152.1) and not at C-5 (C-1–C-6, δ131.0 + 1.0 = 132.0, 126.1–7.7 = 118.4, 144.9 + 1.0 = 145.9, 145.6–14.4 = 131.2, 108.0 + 31.4 = 139.4, 120.7–14.4 = 106.3).

EXPERIMENTAL

Isolation of the constituents. Fruits from a specimen of *I. laevis*, situated near the locality Verdum, along the highway leading to San José de Guaviare, Municipality of San Martin, Department of Meta, Colombia, were collected May 1983. A voucher of the same specimen (col 93415), identified by Dr Roberto Jaramillo M., Instituto de Ciencias Naturales, Universidad Nacional de Colombia, was deposited in 1973.

The fruits were separated into aril, mesocarp and kernel. After drying for a week at 50° each of these parts was powdered. Aril (495 g) [ashes 1.5%, fibre 6.5%, fat (light petrol extract) 31.1%, humidity and volatiles (105°) 4.9%, protein 6.4%] was macerated initially with light petrol and then with $CHCl_3$. Both solutions were filtered and evapd leading to two residues, respectively Al (140 g) and A2 (30 g). Mesocarp (1385 g) was treated in the same way leading to residues, respectively Ml (6 g) and M2 (25 g). Kernel (1425 g) was extracted with C_6H_6 in a soxhlet (8 days). The solution was evaporated. The residue (475 g) was partitioned between light petrol and $EtOH-H_2O$ 9:1. The two layers were evapd leading to residues, respectively Kl (460 g) and K2 (10 g). Fractions A1, M1 and K1 were fats. Transesterification of K1 in $MeOH + BF_3$ and GC analysis of the mixture indicated the predominance of myristate, palmitate and oleate methyl esters. Fractions A2, M2 and K2 were submitted to repeated column chromatography coupled with prep. TLC (Si gel). A2 gave **1a** (5.5 g), **1b** (120 mg) and **2a** (130 mg); M2 gave **1a** (4.5 g) and **2a** (40 mg); K2 gave **1a** (450 mg).

2′,4′-Dihydroxy-4,6′-dimethoxydihydrochalcone (**1a**). ^{13}C NMR (20 MHz, Me_2CO-d_6) δ: 134.6 (C-1), 130.1 (2C-2,6), 114.6 (2C-3, 5), 158.9 (C-4), 46.6 (C-α), 30.7 (C-β), 205.0 (C=O), 105.0 (C-1′), 164.5 (C-2′), 97.0 (C-3′), 165.7 (C-4′), 92.0 (C-5′), 168.2 (C-6′), 55.5, 56.1 (2 OMe). For other data and data on derivatives see ref. [2].

2′,4′,6′-Trihydroxy-4-methoxydihydrochalcone (**1b**). Mp 202–204° (Me_2CO). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 228, 287 (ε28 300, 24 550); $\lambda_{\max}^{\mathrm{MeOH+NaOMe}}$ nm: 226, 248, 322 (ε29 050, 12 000, 32 850); $\lambda_{\max}^{\mathrm{MeOH+AlCl_3}}$ nm: 225, 312 (ε33 350, 32 350). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3330 (OH), 1640 (OH . . O=C), 1620, 1520 (Ar), 830. ^1H NMR (60 MHz, Me_2CO-d_6) δ: 7.18, 6.80 (AA′BB′, *J ca* 8.6 Hz, 2H-2,6, 2H-3,5), 5.92 (s, 2H-3′,5′), 3.35 (*m*, 2H-α), 2.90 (*m*, 2H-β), 3.74 (*s*, OMe); ^{13}C NMR (20 MHz, Me_2CO-d_6) δ: 134.7 (C-1), 130.1 (2C-2,6), 114.6 (2C-3,5), 158.9 (C-4), 46.6 (C-α), 30.7 (C-β), 205.4 (C=O), 105.2 (C-1′), 165.4 (2C-2′,6′), 95.9 (2C-3′,5′), 165.3 (C-4′), 55.4 (OMe). MS (2O eV) *m/z* (rel. int.): 290 $[M+2]^+$ (1), 289 $[M+1]^{+\cdot}$ (7), 288 $[M]^{+\cdot}$ (37), 153 (18), 135 (5), 134 (30), 126 (52), 121 (100). *Triacetate* (**1c**), gum. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1770 (OAc), 1700 (C=O), 1610, 1510 (Ar). ^1H NMR (60 MHz, $CDCl_3$) δ: 6.3–7.2 (*m*, 6H-2,3,5,6,3′,5′), 2.6–3.6 (*m*, 4H-α,β), 3.70 (*s*, OMe), 2.1 (*s*, 2OAc), 2.25 (*s*, OAc). MS (70 eV) *m/z* (rel. int.): 414 $[M]^{+\cdot}$ (17), 372 (7), 354 (11), 330 (8), 312 (15), 288 (4), 270 (21), 237 (43), 195 (57), 153 (79), 135 (12), 134 (68), 121 (98).

3′-(7″-Allylphenyl)-2′,4′,4″-trihydroxy-4,6′-dimethoxy-dihydrochalcone (**2a**). Mp 129–130° ($CHCl_3$). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 225, 290 (ε38450, 23500); $\lambda_{\max}^{\mathrm{MeOH+AlCl_3}}$ no shift; $\lambda_{\max}^{\mathrm{MeOH+NaOMe}}$ nm: 226, 254, 333 (ε 74550, 9950, 27350). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3330 (OH), 1675 (OH. . . O=C), 1610, 1515, 1440 (Ar), 830. ^1H NMR (60 MHz, Me_2CO-d_6) δ: 7.15, 6.75 (AA′BB′, *J ca* 8.6 Hz, 2H-2,6, 2H-3,5), 6.17 (*s*, H-5′), 2.6–3.4 (*m*, 4H-α,β), 3.75, 3.85 (2*s*, 2OMe), 14.55 (*s*, OH. . . O=C), 7.20, 6.85 (AA′BB′, *J ca* 8.6 Hz, 2H-2″,6′, 2H-3″,5″), 6.0–6.6 (*m*, H-8″), 4.95–5.02 (m, H-7″, 2H-9″). ^{13}C NMR (20 MHz, Me_2CO-d_6) δ: 134.6 (C-1), 130.1 (2C-2,6), 114.6 (2C-3,5), 158.9 (C-4), 46.7 (C-α), 30.7 (C-β), 205.0 (C=O), 105.7 (C-1′), 162.6 (C-2′), 114.8 (C-3′), 163.1 (C-4′), 91.8 (C-5′), 165.8 (C-6′), 135.3 (C-1″), 129.3 (2C-2″, 6″), 115.4 (2C-3″,5″), 156.1 (C-4″), 44.1 (C-7″), 141.0 (C-8″), 111.3 (C-9″), 55.4, 55.9 (2 OMe). MS (20 eV) *m/z* (rel. int.): 434 $[M]^{+\cdot}$ (10), 302 (25), 272 (19), 167 (26), 135 (12), 134 $[HOC_6H_4CH_2CH{=}CH_2]^{+\cdot}$ (100), 121 (20). MS (70 eV) *m/z* (rel. int.): 434 $[M]^{+\cdot}$ (1), 302 (4), 272 (6), 167 (53), 135 (9), 134 (62), 121 (100). Hydrogenation of **2a** (68 mg) in C_6H_6 (5.6 ml) in presence of 10% Pd/C, added as a suspension in C_6H_6 (3 ml), gave **2b** (65 mg).

3′-(7″-Propylphenyl)-2′,4′,4″-trihydroxy-4,6′-dimethoxy-dihydrochalcone (**2b**), gum. ^1H NMR (60 MHz, Me_2CO-d_6) δ: 7.07, 6.63 (AA′BB′, J *ca* 8.6 Hz, 2H-2,6, 2H-3,5), 6.0 (*s*, H-5′), 2.6–3.4 (*m*, 4H-α,β), 3.75, 3.85 (2*s*, 2OMe), 13.89 (*s*, OH. . . O =C), 7.15, 6.78 (AA′BB′, J *ca* 8.6, 2H-2″,6″, 2H-3″,5″), 4.40 (*t*, *J* = 8 Hz, H-7″), 1.95–2.45 (*m*, 2H-8″), 0.83 (*t*, *J* = 8 Hz, 3H-9″). ^{13}C NMR (20 MHz, Me_2CO-d_6) δ: 134.6 (C-1), 130.1 (2C-2,6), 114.6 (2C-3,5), 158.9 (C-4), 46.8 (C-α), 30.3 (C-β), 205.4 (C=O), 105.7 (C-1′), 162.2 (C-2′), 112.0 (C-3′), 163.4 (C-4′), 91.7 (C-5′), 166.4 (C-6′), 137.1 (C-1″), 129.8 (2C-2″,6″), 115.2 (2C-3″,5″), 155.8 (C-4″), 41.5 (C-7″), 25.6 (C-8″), 13.4 (C-9″), 55.4, 55.9 (2 OMe). MS (20 eV) *m/z* (rel. int.): 436 $[M]^{+\cdot}$ (7), 407 (19), 302 (10), 167 (32), 134 (100), 121 (29).

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