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FLAVONOIDS FROM *IRYANTHERA LAEVIS**

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Key Word Index—*Iryanthera laevis*; Myristicaceae; dihydrochalcone; flavans; 1,3-diarylpropanes.

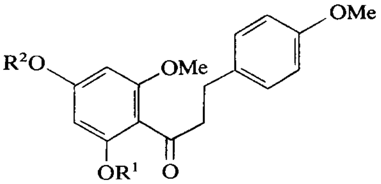
Abstract—Trunk wood of *Iryanthera laevis* Markgr. (Myristicaceae) contains 2′,4′-dihydroxy-4,6′-dimethoxydihydrochalcone, three 2′-hydroxy-4′,5′-methylenedioxyflavans with differently substituted A-rings (7-OH-6,8-diMe; 7-OH-5,8-diMe; 5-OH-7-OMe-6,8-diMe) and 1-(2′-hydroxy-4′-methoxy-5′-methylphenyl)-3-(2″-hydroxy-4″,5″-methylenedioxphenyl)-propane, as well as three additional known diarylpropanes.

INTRODUCTION

Iryanthera laevis Markgr. (Myristicaceae), a tree which may attain a height of 25 m, occurs in central Amazonia [2]. A sample of trunk wood of a specimen, collected in the vicinity of Manaus, yielded besides sitosterol, 7 flavonoids which were classified by trivial ^{1}H NMR assignments into dihydrochalcone [3], flavan [4] and 1,3-diarylpropane [5] types.

RESULTS

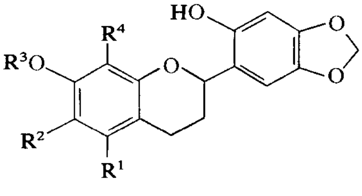
Determination of the MW by MS, allied to hydrogen, carbon, hydroxyl and methoxyl counts by NMR, revealed the formula $C_{15}H_{10}O(OH)_2(OMe)_2$ for the dihydrochalcone. The 6 aromatic protons form AA′BB′ and AB ($J = 2$ Hz) systems consistent only with the oxygenation pattern shown in **1a**. The relative placement of the hydroxyls and the methoxyls relied on the MS and the fact that only one hydroxyl is easily methylated. The other hydroxyl in **1a** and in the methyl ether (**1c**) is chelated ($AlCl_3$ UV shifts). Its acetylation leads to unsymmetrical acetates (**1b**, **1d**), a fact which confirms structure **1a** for the natural compound.



1a $R^1 = R^2 = H$
1b $R^1 = R^2 = Ac$
1c $R^1 = H, R^2 = Me$
1d $R^1 = Ac, R^2 = Me$

All three flavans, $C_{15}H_8O(OH)_2O_2CH_2 \cdot Me_2$ (**2a**, **2b**) and $C_{15}H_7O(OH)_2O_2CH_2 \cdot OMe \cdot Me_2$ (**2c**), possess identically substituted B-rings, as shown in **2**. Indeed, not only does the base peak at *m/e* 164 of all three MS reveal $OH \cdot O_2CH_2$-substitution of the retro Diels–Alder styryl fragment, but the presence only of singlets in the ^{1}H NMR spectra excludes any but the 2′-OH-4′,5′-O_2CH_2-arrangement. As a further common feature of **2a** and **2b**, the presence of the additional hydroxyl at C-7 was assumed on biogenetical grounds. Only constitutions **2a** and **2b** can thus be written for these isomers. A third alternative, with the C-methyls at C-5 and C-6 need not be considered, since allylic coupling of the lone A-ring protons to one of these methyls can be demonstrated for both compounds from ^{1}H NMR experiments. In order to assign formulae to these compounds, **2d** is a suitable model. Its three A-ring H signals occur at τ 3.05 (H-5), 3.48 (H-6) and 3.60 (H-8) in $CDCl_3$ [4], evidence that the 3.25 signal (also in $CDCl_3$) of **2a** refers to H-5, slightly shielded by the *ortho*- and *para*-related C-methyls. The 3.34 signal of **2b** thus must refer to H-6 by default. Here comparison is not as valid since the spectrum was taken in $(CD_3)_2CO$.

With respect to the third flavan, it is again reasonable to assume the presence of an oxy-function at C-7 and, since here the acetate derived ring is fully substituted, also at C-5. Acetylation of the hydroxyl affects



2a $R^1 = R^3 = H, R^2 = R^4 = Me$
2b $R^1 = R^4 = Me, R^2 = R^3 = H$
2c $R^1 = OH, R^2 = R^3 = R^4 = Me$
2d $R^1 = R^2 = R^4 = H, R^3 = Me$

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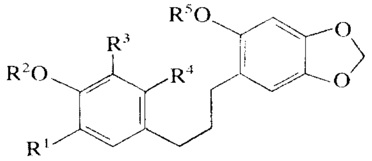
*Part 14 in the series "The Chemistry of Brazilian Myristicaceae". For Part 13 see ref. [1]. Based on the M.S. Thesis submitted by M. S. da S. to Universidade Federal Rural do Rio de Janeiro (1979).

the two C-methyls differently. Their originally superimposed signals at τ 8.00 shift to 8.04 and 7.95. A symmetrical arrangement of the methyls with respect to the hydroxyl thus becomes improbable, and formula **2c** is proposed for the natural compound.

Among the four 1,3-diarylpropanes, **3a–c** are known compounds, having been isolated respectively from *Iryanthera coriacea* Ducke [5] and *I. polyneura* Ducke [3]. The substitution pattern of the fourth 1,3-diarylpropane $C_{15}H_{10}(OH)_2OMe{\cdot}O_2CH_2{\cdot}Me$ was again elucidated initially by MS. This, through an outstandingly intense tropylium peak at *m/e* 151 (100%) [accompanied by a quinone methide peak of moderate intensity at *m/e* 150 (8%)], indicated the generation of ions of equal masses by both benzylic cleavages, thus assigning $OH{\cdot}O_2CH_2$ functions to one ring and OH·OMe·Me groups to the other. Chemical shifts and multiplicities (all singlets) of the NMR signals due to the aromatic protons locate these substituents unequivocally as shown in **3d** or **3e**. The compound represented by **3d** bears 2′- and 2″-hydroxyls and its MS should contain, besides the tropylium peak, a strong quinone methide peak (cf. intensity relation for *m/e* 151/150 peaks of model **3f**: 100/30 [5]). In view of the intensity ratio stated above, formula **3e** becomes thus somewhat more plausible as representation of the natural compound (cf. intensity relation for *m/e* 151/150 peaks of model **3g**: 100/12 [5]).



3a $R^1 = R^2 = R^3 = H$, $R^4 = OH$, $R^5 = Me$
3b $R^1 = R^2 = H$, $R^4 = OH$, $R^2 = R^5 = Me$
3c $R^1 = R^3 = Me$, $R^2 = R^5 = H$, $R^4 = OH$
3d $R^1 = R^2 = Me$, $R^3 = R^5 = H$, $R^4 = OH$
3e $R^1 = Me$, $R^2 = R^3 = R^5 = H$, $R^4 = OMe$
3f $R^1 = R^3 = Me$, $R^2 = R^5 = H$, $R^4 = OH$
3g $R^1 = R^3 = R^4 = R^5 = H$, $R^2 = Me$

DISCUSSION

Iryanthera laevis, like the other six species of the genus so far examined [6], proved to be a rich source of flavans and 1,3-diarylpropanes, compound types whose biosynthetic connection has been postulated [7]. No neolignans were so far isolated from any *Iryanthera* species. By contrast, in the geographically and morphologically related genus *Virola*, flavans have not yet been found and 1,3-diarylpropanes show comparatively slight structural variation, while neolignans are widespread [6].

EXPERIMENTAL

Isolation of the constituents. Trunk wood of *Iryanthera laevis* was collected near Manaus, Amazonas State, and identified by the botanist Dr. William A. Rodrigues. An EtOH extract (2%, 100 g) was adsorbed on Si gel (450 g). The resulting dry powder, washed successively with petrol, C_6H_6 and $CHCl_3$ gave respectively eluates A, B and C. A (15 g) was cryst. to sitosterol (4 g). B (20 g) was chromatographed on Si gel (500 g). Elution with C_6H_6–MeOH 100:0, 99:1, 98:2, 95:5, 92:8 and 90:10 gave 6 fractions which were rechromatographed giving in order sitosterol and **1a**; **1a** and **2a**; **2a**; **2a** and **2b**; **2b**; **2b** and **2c**. C (30 g) was chromatographed on Si gel (900 g). Elution with $CHCl_3$–Me_2CO 100:0, 99:1, 97:3, 95:5 and 90:10 gave 5 fractions which were rechromatographed giving in order **1a**, **2a**, **2b**, **2c** and **3c**; **2b** and **3c**; no pure material; **3d** and **3b**; **3b** and **3a**. Approximate quantities obtained: sitosterol 5 g, **1a** 90 mg, **2a** 15 mg, **2b** 40 mg, **2c** 30 mg, **3a** 18 mg, **3b** 25 mg, **3c** 190 mg, **3e** 30 mg.

Identifications of the known **3a** [5], **3b** [3], **3c** [5] were performed by direct comparison with authentic samples.

2′,4′-Dihydroxy-4,6′-dimethoxydihydrochalcone (**1a**). Mp 182–184° (C_6H_6). ν_{max}^{KBr} cm^{-1}: 2400–3100, 3300, 1630, 1620, 1570, 1520, 1470, 800. λ_{max}^{EtOH} nm: 224, 290 (ε 27 800, 23 850); $\lambda_{max}^{EtOH+NaOH}$ nm: 210, 245, 332 (ε 36 000, 9950, 43 200); $\lambda_{max}^{EtOH+AlCl_3}$ nm: 220, 308 (ε 31 700, 22 950). ^{1}H NMR (100 MHz, Me_2CO-d_6): τ 6.72, 7.12 (2 *ca t*, $J = 7.5$ Hz, 2 H-β, 2 H-α), 6.23, 6.10 (2 *s*, 2 OMe), 4.03, 3.96 (2 *d*, $J = 2$ Hz, H-5′, H-3′), 3.16, 2.80 (AA′BB′ system, $J = 9$ Hz, H-3, H-5; H-2, H-6), −3.66 (*s*, OH-2′). ^{13}C NMR (20 MHz, Me_2CO-d_6): δ 30.7 (*t*, C-β), 46.6 (*t*, C-α), 55.9 (*q*, 2 OMe), 91.9, 96.9, 114.6, 130.1 (4 *d*. respectively C-5′, C-3′, C-3 + C-5, C-2 + C-6), 206.8 (*s*, C=O). MS (*m/e*): 302 (37%) M^+, 168 (10), 167 (97), 152 (8), 135 (12), 134 (100), 121 (60).

Diacetate (**1b**). Mp 92–94° (MeOH). ν_{max}^{film} cm^{-1}: 1780, 1700, 1615, 1510, ^{1}H NMR (100 MHz, $CDCl_3$): τ 7.84, 7.70 (2 *s*, 2 OAc), 6.90, 7.06 (2 *ca t*, $J = 6.0$ Hz, 2 H-β, 2 H-α), 6.20 (*s*, 2 OMe), 3.43, 3.38 (2 *d*. $J = 2$ Hz, H-5′, H-3′), 3.16, 2.84 (AA′BB′ system, $J = 9$ Hz, H-3, H-5; H-2, H-6). MS (*m/e*): 386 (47%) M^+, 344 (10), 327 (28), 302 (8), 168 (13), 167 (100), 135 (25), 134 (92), 121 (75).

Methyl ether (**1c**). Mp 130° (MeOH). ν_{max}^{film} cm^{-1}: 1690, 1615, 1510. λ_{max}^{EtOH} nm: 224, 287 (ε 14 500, 12 700): $\lambda_{max}^{EtOH+AlCl_3}$ nm: 220, 307 (ε 16 600, 12 100). ^{1}H NMR (60 MHz, $CDCl_3$): τ 6.60–7.20 (2 *m*, 2 H-β, 2 *H*-α) 5.20 (*s*, OMe), 6.14 (*s*, 2 OMe), 4.04, 3.90 (2 *d*, $J = 2$ Hz, H-5′, H−3′), 3.12, 2.80 (AA′BB′ system, $J = 9$ Hz, H-3, H−5; H-2, H-6), −4.0 (*s*, OH-2′). MS (*m/e*): 316 (85%) M^+, 182 (28), 181 (100), 166 (15), 135 (30), 134 (100), 121 (95).

Acetate of methyl ether (**1d**). Mp 75°. ν_{max}^{film} cm^{-1}: 1775, 1765, 1685, 1610, 1585, 1505. ^{1}H NMR (60 MHz, CCl_4): τ 7.90 (*s*, OAc-2′), 7–7.2 (*m*, 2 CH_2), 6.24 (*s*, OMe), 6.20 (*s*, 2 OMe), 3.82, 3.70 (2 *d*, $J = 2$ Hz, H-5′, H-3′), 3.24, 2.90 (AA′BB′ system, $J = 9$ Hz, H-3, H-5; H-2, H-6). MS (*m/e*): 358 (8%) M^+, 182 (12), 181 (100), 151 (80), 134 (70), 121 (36).

7,2′-Dihydroxy-6,8-dimethyl-4′,5′-methylenedioxyflavan (**2a**). Mp 168–170° (C_6H_6) (Found: M, 314.1119. $C_{18}H_{18}O_5$ requires: M, 314.1154). ν_{max}^{film} cm^{-1}: 3520, 3350, 1610, 1490. λ_{max}^{EtOH} nm: 230, 293 (ε 19900, 9000); $\lambda_{max}^{EtOH+NaOH}$ nm: 232, 308, (19900, 9350). ^{1}H NMR (100 MHz, $CDCl_3$): τ 7.9–7.6 (*m*, 2 H−3), 7.88, 7.80 (2 *s*, 2 ArMe), 7.2–7.0 (*m*, 2 H-4), 4.94 (*dd*, $J = 10$, 6 Hz, H-2), 4.08 (*s*, O_2CH_2), 3.50, 3.38 (2 *s*, H-3′, H-6′), 3.25 (*br. s*, H-5), 3.04 (*br. s*, 2 OH). MS (*m/e*): 314 (30%) M^+, 177 (8), 164 (100), 163 (20), 151 (88), 150 (7), 149 (6), 135 (9). *Diacetate*, mp 125°. ν_{max}^{film} cm^{-1}: 1770, 1615, 1505, 1490. MS (*m/e*): 398 (15%) M^+, 356 (38), 314 (9), 206 (85), 192 (12), 191 (37), 164 (100), 151 (42), 150 (13), 149 (40).

7,2′-Dihydroxy-5,8-dimethyl-4′,5′-methylenedioxyflavan (**2b**). Mp 174–176° (C_6H_6–petrol) (Found: M, 314.1165. $C_{18}H_{18}O_5$ requires: M, 314.1154). ν_{max}^{film} cm^{-1}: 3550, 3450, 1620, 1495. λ_{max}^{EtOH} nm: 237, 280, 350 (ε 24 500, 13 800, 12 350); $\lambda_{max}^{EtOH+NaOH}$ nm: 245, 280, 385 (ε 22 600, 14 450 12 650). ^{1}H NMR (100 MHz, $CDCl_3$ + Me_2CO-d_6): τ 8.2–7.7

(*m*, 2 H-3), 7.86, 7.80 (2 *s*, 2 ArMe), 7.3–7.0 (*m*, 2 H-4), 4.82 (*dd*, $J = 9$, 3 Hz, H-2), 4.1 (*s*, O_2CH_2), 3.54, 3.22 (2 *s*, H-3′, H-6′), 3.34 (*br. s*, H-6), 3.92, 2.42 (2 *br. s*, 2-OH). MS (*m*/*e*): 314 (36%) M^+, 177 (10), 164 (100), 163 (11), 151 (58), 149 (12), 137 (6). *Diacetate*, mp 112° (CCl_4). ν_{max}^{KBr} cm^{-1}: 1760, 1600, 1500, 1490. ^{1}H NMR (100 MHz, $CDCl_3$): τ 8.2–7.8 (*m*, 2 H-3), 8.00, 7.90 (2 *s*, 2 ArMe), 7.73, 7.65 (2 *s*, 2 OAc), 7.3–7.0 (*m*, 2 H-4), 4.98 (*dd*, $J = 9$, 3 Hz, H-2), 4.0 (*s*, O_2CH_2), 3.38, 3.00 (2 *s*, H-3′, H-6′), 3.20 (*br. s*, H-6). MS (*m*/*e*): 398 (30%) M^+, 356 (66), 314 (15), 177 (8), 164 (100), 151 (58).

5,2′-*Dihydroxy-7-methoxy*-6,8-*dimethyl*-4′,5′-*methylenedioxyflavan* (**2c**). Mp 164–166° (C_6H_6) (Found: M, 344.1249. $C_{19}H_{20}O_6$ requires: 344.1260). ν_{max}^{film} cm^{-1}: 3430, 1605, 1500. λ_{Max}^{EtOH} nm: 287, 301 (ε 25 450, 32 700). $\lambda_{max}^{EtOH+NaOH}$ nm: 287, 312 (ε 19 950, 27 500). ^{1}H NMR (60 MHz, CCl_4): τ 8.2–7.8 (*m*, 2 H-3), 8.0 (*s*, 2 ArMe), 7.4–7.0 (*m*, 2 H-4), 6.30 (*s*, OMe), 5.0 (*dd*, $J = 8$, 4 Hz, H-2), 4.15 (*s*, O_2CH_2), 3.60, 3.38 (2 *s*, H-3′, H-6′). MS (*m*/*e*): 344 (38%) M^+, 181 (100), 180 (10), 165 (47), 164 (80), 163 (11), 152 (13), 151 (78), 150 (69), 121 (60). *Diacetate*, mp 125–127° (MeOH). ν_{max}^{film} cm^{-1}: 1760, 1600, 1495. ^{1}H NMR (100 MHz, $CDCl_3$): τ 8.2–7.8 (*m*, 2 H-3), 8.04, 7.95 (2 *s*, 2 ArMe), 7.74, 7.66 (2 *s*, 2 ArOAc), 7.3–7.0 (*m*, 2 H-4), 6.28 (*s*, OMe), 4.02 (*s*, O_2CH_2), 3.42, 3.02 (2 *s*, H-3′, H-6′). MS (*m*/*e*): 428 (3%) M^+, 386 (8), 344 (10), 181 (15), 165 (8), 164 (12), 151 (20), 43 (100).

1-(2′-*Hydroxy*-4′-*methoxy*-5′-*methylphenyl*)-3-(2″-*hydroxy*-4″,5″-*methylenedioxyphenyl*)-*propane* (**3e**). Viscous oil (Found: M, 316.1301. $C_{18}H_{20}O_5$ requires: 316.1311). ν_{max}^{film} cm^{-1}: 3400, 1610, 1500, 1480. λ_{max}^{EtOH} nm: 295 (ε 18 350); $\lambda_{max}^{EtOH+NaOH}$ nm: 303 (ε 19 900). ^{1}H NMR (60 MHz, $CDCl_3$): τ 8.3–8.0 (*m*, 2 H-2), 7.83 (*s*, ArMe), 7.6–7.3 (*m*, 2 H-1, 2 H-3), 6.22 (*s*, OMe), 4.1 (*s*, O_2CH_2), 3.58, 3.34 (2 *s*, H-3′+H-3″, H-6″), 3.10 (*br. s*, H-6′). MS (*m*/*e*): 316 (48%) *M*$^+$, 178 (30), 165 (36), 164 (26), 163 (8), 152 (22), 151 (100), 150 (8), 148 (15), 137 (10), 135 (12), 134 (12), 121 (27). *Diacetate*, oil. ν_{max}^{film} cm^{-1}: 1770, 1615, 1505, 1490. ^{1}H NMR (100 MHz, $CDCl_3$): τ 8.3–7.9 (*m*, 2 H-2), 7.9 (*s*, ArMe), 7.80, 7.66 (2 *s*, 2OAc), 7.7–7.3 (*m*, 2 H-1, 2 H-3), 6.22 (*s*, OMe), 4.04 (*s*, O_2CH_2), 3.47, 3.28 (2 *s*, H-3′+H−3″, H−6″), 3.05 (*br. s*, H-6′). MS (*m*/*e*): 400 (11%) M^+, 358 (46), 316 (36), 178 (18), 165 (22), 164 (20), 152 (15), 151 (100), 149 (28), 137 (13), 134 (37), 121 (50).

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