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FLAVONOLIGNOIDS FROM FRUITS OF *IRYANTHERA GRANDIS**

DULCE H. S. SILVA, ALBERTO J. CAVALHEIRO, MASSAYOSHI YOSHIDA and OTTO R. GOTTLIEB†

Instituto de Química, Universidade de São Paulo, 05508-900 São Paulo, SP, Brazil

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Key Word Index—*Iryanthera grandis*; Myristicaceae; fruits; flavonolignoids; stereochemistry.

Abstract—Fruits of *Iryanthera grandis* were found to contain two new pairs of diastereoisomeric flavonolignoids of the 1,4-diaryl-2,3-dimethyl-*n*-butyldihydrochalcone type.

INTRODUCTION

Iryanthera grandis belongs to the Myristicaceae, a family rich in neolignans and flavonoids. Its fruits have been reported to contain the dihydrochalcone **1** and neolignan **2**, besides tocotrienols and a juruenolide [2, 3]. The present work describes the occurrence in the same species of two new pairs of diastereoisomeric flavonolignoids, namely **3** and **4** (iryantherins G and H) and **5** and **6** (iryantherins I and J). Other species of *Iryanthera* (*I. laevis*, *I. ulei* and *I. paraensis*) have already been reported to contain flavonolignoids [4, 5]. Compounds **3**–**6** belong to the structural type represented by iryantherin B (**7**), previously isolated from *I. ulei* bark [5].

RESULTS AND DISCUSSION

The comparison of the ^{1}H and ^{13}C NMR spectra of iryantherin G acetate (**3a**) with those of iryantherin B acetate (**7a**) (Tables 1–4) led to the identification of **3a** as 15-de-*O*-methyl-15-*O*-acetyl-**7a**. The presence of only one methoxyl group shown by ^{1}H (δ3.78) and ^{13}C (δ55.2) NMR spectra allied to mass spectral data ([M]$^+$ *m/z* 766 and ions a, b, c) confirmed the position of this methoxyl group on ring D and the proposed structure for **3a**. All assignments for the aliphatic protons of the lignoid unit of **3a** were confirmed by ^{1}H–^{1}H shift-correlated 2D NMR spectroscopy (Table 5).

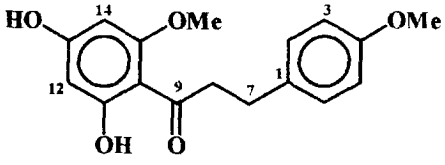
The structural determination of **4a** was based on comparison of its ^{1}H and ^{13}C NMR spectral data with those of **3a**. Significant differences were observed only for the chemical shifts of the chiral carbons 7′, 8′, 8″ as well as for protons and carbons attached to or near chiral centres. Thus **3a** and **4a** should form a pair of diastereoisomers. Chemical shift assignments for the aliphatic protons of the lignoid unit in **4a** were based on ^{1}H–^{1}H shift-correlated 2D spectroscopy (Table 6).

The differential NOE spectra of **3a** and **4a** showed enhancement of signals for the Me-9″ and Me-9′ groups when the methyne proton at C-7′ and the methylene protons at C-7″ were irradiated, respectively. Conversely, H-7′ and 2H-7″ had their signals increased upon irradiation of Me-9″ and Me-9′, respectively. These observations indicate the spatial vicinity of 2H-7″ and Me-9′ and of a *syn*-periplanar relationship between H-7′ and Me-9″. These requisites, allied to the *anti*-periplanar relationship between H-7′ and H-8′, evidenced by application of the Karplus equation to their coupling constant (J = 11.1 Hz), gives the molecules a relative rigidity. This excludes stereochemical arrangements where the configurations of C-8′ and C-8″ are both *R* or both *S* and leads to only two possible alternatives, rel-7′*R*,8′*R*,8″*S* (I) and rel-7′*S*,8′*R*,8″*S* (II). Localization in the shielding cones of rings A and B provides relative protection to Me-9′ in I and to Me-9″ in II. Hence, the ^{1}H and ^{13}C NMR chemical shifts at relatively high field for Me-9′ in the spectra of **3a** (and **7a**), and for Me-9″ in the spectra of **4a**, establish the respective configurations I and II for these compounds.

Structural determinations of **5a** and **6a** were based on comparison of their ^{1}H (Tables 1 and 3) and ^{13}C NMR (Tables 2 and 4) spectra which proved to be closely similar to those of **3a** and **4a**, respectively, except for signals due to the presence of a methylenedioxy group in the former versus a methoxy group in the latter. Mass spectral data showed peaks for ions a, b and c, which confirmed the position of the methylenedioxyl on ring D. Chemical shift assignments of the lignoid aliphatic protons of **5a** and **6a** were based on ^{1}H–^{1}H shift-correlated 2D spectroscopy (Tables 7 and 8). As in the case of **3a** and **4a**, comparison of NMR data led to stereochemical proposals for the relative configuration of structure **5a** as rel-7′*R*,8′*R*,8″*S* and **6a** as rel-7′*S*,8′*R*,8″*S*.

*Part 37 in the series 'The Chemistry of Brazilian Myristicaceae'. For Part 36, see ref. [1]. Based in part on the M. S. thesis presented by D.H.S.S. to Universidade de São Paulo (1993).

†Present address: Departamento de Fisiologia e Farmacodianâmica, Instituto Oswaldo Cruz, Fiocruz, Rio de Janeiro, RJ, Brazil.



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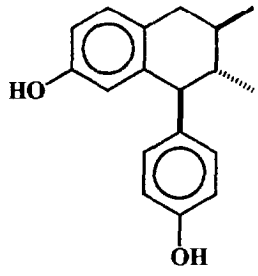

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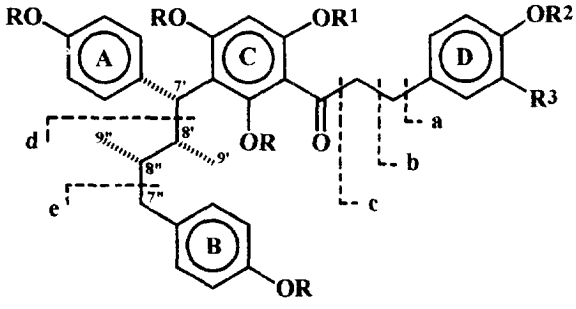
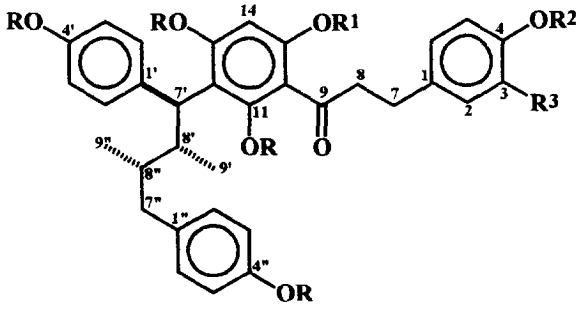


I

3	R=R^1=R^3=H, R^2=Me
3a	R=R^1=Ac, R^2=Me, R^3=H
5	R=R^1=H, R^2-R^3=CH$_2$O
5a	R=R^1=Ac, R^2-R^3=CH$_2$O
7	R=R^3=H, R^1=R^2=Me
7a	R=Ac, R^1=R^2=Me, R^3=H



II

4	R=R^1=R^3=H, R^2=Me
4a	R=R^1=Ac, R^2=Me, R^3=H
6	R=R^1=H, R^2-R^3=CH$_2$O
6a	R=R^1=Ac, R^2-R^3=CH$_2$O

From the biosynthetic point of view, it is interesting to note that the lignoid unit of iryantherins G–J is the *seco*-derivative of the aryltetraline (**2**). The flavonoid unit of iryantherins G–J is the 15-de-*O*-methyl-dihydrochalcone (**1**) previously isolated from the fruits of *I. laevis* [4], but not from the fruits of *I. grandis* [2, present work].

EXPERIMENTAL

Isolation of constituents. Fruits of *I. grandis* Ducke were collected near Itaituba, Pará State, by Dr Hipólito Ferreira Paulino Filho and identified by Dr William Rodrigues. Fruits were dried, powdered and extracted first with hexane and then with EtOH. The EtOH extract (2 g) was partitioned with hexane, $CHCl_3$, EtOAc and MeOH. The $CHCl_3$ phase (802 mg) was submitted to CC over silica gel ($CHCl_3$–EtOAc–MeOH, 49.5:49.5:1) resulting in 10 frs. Acetylation and two-step HPLC analysis of fr. 6 (50 mg) (1st step: Si-60 column 250 × 22 mm, 10 μ-Perkin Elmer; CH_2Cl_2–isoPrOH; 99.4:0.6; 2nd step: C-18 RAC II column 100 × 4.6 mm, 5 μ-Whatman; MeCN–H_2O; 53:47) gave **3a** (3 mg), **4a** (2 mg), **5a** (2 mg) and **6a** (2 mg).

Iryantherin G pentaacetate (**3a**). ^{1}H NMR: Tables 1 and 3. ^{13}C NMR: Tables 2 and 4. MS (70 eV) *m/z* (rel. int.): 766 ([M]$^+$, 1), 561 ([M − d]$^+$, 4), 519 ([M − d − 42]$^+$, 14), 477 ([M − d − 84]$^+$, 26), 435 ([M − d − 126]$^+$, 26), 393 ([M − d − 168]$^+$, 18), 135 ([c]$^+$, 5), 134 ([c − 1]$^+$, 8), 121 ([b]$^+$, 100), 107 ([a]$^+$, 64).

Iryantherin H pentaacetate (**4a**). ^{1}H NMR: Tables 1 and 3. ^{13}C NMR: Tables 2 and 4. MS (70 eV) *m/z* (rel. int.): 766 ([M]$^+$, 0), 561 ([M − d]$^+$, 4), 519 ([M − d − 42]$^+$, 13), 477 ([M − d − 84]$^+$, 23), 435 ([M − d − 126]$^+$, 24), 393 ([M − d − 168]$^+$, 18), 135 ([c]$^+$, 13), 134 ([c − 1]$^+$, 11), 121 ([b]$^+$, 100), 107 ([a]$^+$, 66).

Iryantherin I pentaacetate (**5a**). ^{1}H NMR: Tables 1 and 3. ^{13}C NMR: Tables 2 and 4. MS (70 eV) *m/z* (rel. int.): 780 ([M]$^+$, 0), 575 ([M − d]$^+$, 3), 533 ([M − d − 42]$^+$, 16), 491 ([M − d − 84]$^+$, 31), 449 ([M − d − 126]$^+$, 27), 407 ([M − d − 168]$^+$, 16), 149 ([c]$^+$, 6) 148 ([c − 1]$^+$, 14), 135 ([b]$^+$, 100), 121 ([a]$^+$, 17), 107 ([e − 42]$^+$, 75).

Iryantherin J pentaacetate (**6a**). ^{1}H NMR: Tables 1 and 3. ^{13}C NMR: Tables 2 and 4. MS (70 eV) *m/z* (rel. int.): 780 ([M]$^+$, 0), 575 ([M − d]$^+$, 3), 533 ([M − d − 42]$^+$, 18), 491 ([M − d − 84]$^+$, 31), 449 ([M − d − 126]$^+$, 28), 407 ([M − d − 168]$^+$, 16), 149 ([c]$^+$, 8), 148 ([c − 1]$^+$, 13), 135 ([b]$^+$, 100), 121 ([a]$^+$, 17), 107 ([e − 42]$^+$, 74).

Table 1. ^{1}H NMR data for flavonoid units of iryantherin acetates

H	3a	4a	5a	6a	7a [5]
2,6	6.8–7.2 *m*	7.09 *d*, 8.4	—	—	6.7–7.2 *m*
3,5	6.8–7.2 *m*	6.80 *d*, 8.5	—	—	6.7–7.3 *m*
2,3,5	—	—	6.6–7.2 *m*	6.6–6.8 *m*	—
7	2.9–3.1 *m*	2.8–3.1 *m*	2.8–3.1 *m*	2.7–3.1 *m*	2.9–3.1 *m*
8	2.9–3.1 *m*	2.8–3.1 *m*	2.8–3.1 *m*	2.7–3.1 *m*	2.9–3.1 *m*
14	6.8–7.2 *m*	6.94 *s*	6.6–7.2 *m*	6.95 *s*	6.46 *s*
MeO-4	3.78 *s*	3.76 *s*	—	—	3.69 *s*
MeO-15	—	—	—	—	3.76 *s*
CH_2O_2-3,4	—	—	5.91 *s*	5.91 *s*	—

Table 2. ^{13}C NMR data for flavonoid units of iryantherin acetates

C	3a	4a	6a	7a [5]
1	133.0	133.0	134.9	133.6
2,6	129.5	129.5	108.2/121.2	129.5
3,5	113.9	115.5	147/109.0	113.8
4	158.0	158.0	145.7	157.9
7	28.6	29.7	29.7	29.0
8	45.5	45.2	45.2	45.4
9	200.0	200.1	199.9	201.9
10	129.4	128.2	126.5	122.4
11	145.6	145.7	145.7	—
12	127.6	126.6	126.5	122.4
13	150.0	151.0	149.8	—
14	116.0	115.5	115.5	105.0
15	149.7	148.5	148.8	155.7
MeO-4	55.2	55.2	—	55.3
MeO-15	—	—	—	55.9
CH_2O_2-3,4	—	—	100.8	—

Table 3. ^{1}H NMR data for lignoid units of iryantherin acetates

H	3a	4a	5a	6a	7a [5]
2′,6′	6.8–7.2 *m*	7.13 *d*, 8.7	6.6–7.2 *m*	7.13 *d*, 8.5	6.7–7.3 *m*
2″,6″	6.8–7.2 *m*	7.12 *d*, 8.7	6.6–7.2 *m*	7.09 *d*, 8.6	6.7–7.3 *m*
3′,5′	6.8–7.2 *m*	6.95 *d*, 8.7	6.6–7.2 *m*	6.96 *d*, 8.5	6.7–7.3 *m*
3″,5″	6.8–7.2 *m*	6.90 *d*, 8.7	6.6–7.2 *m*	6.90 *d*, 8.6	6.7–7.3 *m*
7′	4.03 *d*, 11.1	4.09 *d*, 11.2	4.04 *d*, 11.2	4.10 *d*, 11.2	4.10 *d*, 4.3
8′	2.5–2.7 *m*	2.5–2.7 *m*	2.5–2.7 *m*	2.6–2.7 *m*	1.6–2.2 *m*
7″	2.5–2.6 *m*	2.4–2.6 *m*	2.5–2.7 *m*	2.4–2.6 *m*	2.1–2.5 *m*
8″	1.9–2.1 *m*	1.5–1.7 *m*	2.1–1.8 *m*	1.5–1.7 *m*	1.6–2.2 *m*
Me-9′	0.65 *d*, 6.8	0.90 *d*, 6.5	0.64 *d*, 6.9	0.92 *d*, 6.5	0.65 *d*, 6.8
Me-9″	0.85 *d*, 6.2	0.74 *d*, 6.5	0.85 *d*, 6.5	0.76 *d*, 6.6	0.84 *d*, 6.6

Table 4. ^{13}C NMR data for lignoid units of iryantherin acetates

C	3a	4a	6a	7a [5]
1′	138.5[a]	138.4[a]	138.2[a]	138.7
2′,6′	129.4[b]	129.4[b]	129.5[b]	129.5
3′,5′	121.4[c]	121.3[c]	121.3[c]	121.4
4′	149.0[d]	149.0[d]	148.8[d]	148.9
7′	43.8	45.9	45.9	43.5
8′	35.1	35.7	35.7	35.3
9′	10.6	13.4	13.4	10.7
1″	137.9[a]	138.2[a]	138.4[a]	138.7
2″,6″	130.3[b]	130.1[b]	130.1[b]	130.4
3″,5″	121.0[c]	121.0[c]	121.1[c]	120.9
4″	149.1[d]	149.7[d]	149.7[d]	149.2
7″	40.9	41.5	41.5	41.1
8″	32.0	34.3	34.3	32.3
9″	14.0	12.3	12.4	14.0

[a-d]Values with the same letter are interchangeable in the same column.

Table 5. ^{1}H–^{1}H 2D NMR correlations for **3a**

Signals	Correlated H signals
4.03 (H-7′)	2.5–2.7 (H-8′)
2.5–2.6 (H-7″)	1.9–2.1 (H-8″)
2.5–2.7 (H-8′)	0.65 (H-9′), 1.9–2.1 (H-8″), 4.03 (H-7′)
1.9–2.1 (H-8″)	0.85 (H-9″), 2.5–2.6 (H-7″)
0.85 (H-9″)	1.9–2.1 (H-8″)
0.65 (H-9′)	2.5–2.6 (H-7″)

Table 6. ^{1}H–^{1}H 2D NMR correlations for **4a**

Signals (H)	Correlated H signals
4.09 (H-7′)	2.5–2.7 (H-8′)
2.5–2.7 (H-8′)	0.90 (H-9′), 4.09 (H-7′)
1.5–1.7 (H-8″)	0.74 (H-9″)
0.90 (H-9′)	2.5–2.7 (H-8′)
0.74 (H-9″)	1.5–1.7 (H-8″)

Table 7. ^1H–^1H 2D NMR correlations for **5a**

Signals (H)	Correlated H signals
4.04 (H-7′)	2.5–2.7 (H-8′)
2.5–2.7 (H-7″)	1.8–2.1 (H-8″)
2.5–2.7 (H-8′)	0.64 (H-9′), 1.82–2.1 (H-8″), 4.04 (H-7′)
1.8–2.1 (H-8″)	0.85 (H-9″), 2.5–2.7 (H-7″)
0.85 (H-9″)	1.8–2.1 (H-8″)
0.64 (H-9″)	2.5–2.7 (H-8″)

Table 8. ^1H–^1H 2D NMR correlations for **6a**

Signals (H)	Correlated H signals
4.10 (H-7′)	2.6–2.7 (H-8′)
2.6–2.7 (H-8′)	0.92 (H-9′), 4.10 (H-7′)
2.4–2.6 (H-7″)	1.5–1.7 (H-8″)
1.5–1.7 (H-8″)	0.76 (H-9″), 2.4–2.6 (H-7″)
0.92 (H-9′)	2.6–2.7 (H-8′)
0.76 (H-9″)	1.5–1.7 (H-8″)

Notes to spectral data (*Tables* 1–8). Spectra were obtained in $CDCl_3$ solns. ^1H NMR were recorded at 200 MHz, and ^{13}C NMR at 50 MHz. Additional signals for **3a**: ^1H NMR δ2.08, 2.23, 2.26, 2.31 (5 × AcO); ^{13}C NMR δ20.6, 20.8, 20.9, 21.1, 21.1, 167.5, 167.8, 168.6, 169.4 (5 × AcO). Compound **4a**: ^1H NMR δ2.10, 2.23, 2.28 (5AcO); ^{13}C NMR δ20.9, 21.1, 167.9, 169.5, 169.6 (5 × AcO). Compound **5a**: ^1H NMR δ2.05, 2.19, 2.25 (5 AcO). **6a**: ^1H NMR 2.15, 2.25 2.29 (5 × AcO); ^{13}C NMR δ20.9, 21.1, 167.8, 168.3, 169.4, 169.6 (5 × AcO). In Tables 1 and 3, the coupling constants, registered jointly with signal multiplicities, are in Hz. In all ^{13}C NMR, the *n*-value of CH_n-groups was ascertained by DEPT-135° expts. In Table 4, data marked with letters a, b, c, d may be interchanged with other identically marked data of the same column.

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