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4-ARYLCOUMARINS FROM *COUTAREA HEXANDRA**

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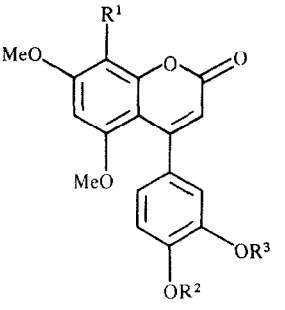
Key Word Index—*Coutarea hexandra*; Rubiaceae; neoflavonoids; 4-arylcoumarins.

Abstract—The structures of two neoflavonoids, isolated from a benzene extract of *Coutarea hexandra* have been established as 3′-hydroxy-5,7,8,4′-tetramethoxy-4-phenylcoumarin and 8,3′-dihydroxy-5,7,4′-trimethoxy-4-phenylcoumarin. The substitution pattern of 8,3′,4′-trihydroxy-5,7-dimethoxy-4-phenylcoumarin, also isolated, was also confirmed by chemical reactions.

INTRODUCTION

Several 5,7-dioxygenated-4-arylcoumarins have been isolated from *Coutarea hexandra* [1–4]. 4-Arylcoumarins containing an extra oxygen in the A ring have also been reported [5, 6] from the same plant as well as from *C. latiflora* [7]. We now report the isolation from a benzene extract of *C. hexandra* and the structural elucidation of further two 8-oxygenated-4-arylcoumarins, **1** and **2**. The structure of a third neoflavonoid (**3**), previously reported from a methanolic extract [6] of the same plant, was confirmed by methylenation and methylation.



	R¹	R²	R³
1	OMe	Me	H
1a	H	Me	H
1b	OMe	Me	Ac
2	OH	Me	H
2a	OAc	Me	Ac
3	OH	H	H
3a	OAc	Ac	Ac
4	OMe	Me	Me
5	OH	—CH_2—	
5a	OMe	—CH_2—	

RESULTS AND DISCUSSION

Compounds **1–3** gave with diazomethane the same permethylated derivative **4**, thus revealing an identical substitution pattern. The 5,7,8-substitution of the A ring was demonstrated by the presence of a high field signal (3H, δ3.50) [8] in the ^{1}H NMR spectrum and of only one resonance at δ 61 in the ^{13}C NMR spectrum [5]. Conversely, the 3′,4′-substitution of the B ring was established by comparison with the ^{1}H and ^{13}C NMR data of analogous compounds [1, 9] and confirmed by methylenation of compound **3** (*vide infra*).

The first compound, $C_{19}H_{18}O_7$ (**1**), was a monohydroxytetramethoxy-4-arylcoumarin, based on spectral evidence. The hydroxy group cannot be located on the A ring because no bathochromic shift (diagnostic for 5- or 7-OH [4]) was observed in the UV spectrum by addition of alkali, while an intense $[M-Me]^+$ ion (due to the 8-OMe [10]) was present in the mass spectrum. The ^{1}H NMR spectra in chloroform-*d* and pyridine-d_5 (60 MHz) indicated a B ring substitution pattern coincident with that of 3′-hydroxy-5,7-4′-trimethoxy-4-phenylcoumarin (**1a**) [1]. Accordingly, the H-2′ and H-6′ signals were shifted downfield by 0.1 and 0.35 ppm, respectively, in the ^{1}H NMR spectrum of the acetyl derivative **1b**. Compound **1** was thus assigned the structure 3′-hydroxy-5,7,8,4′-tetramethoxy-4-phenylcoumarin.

The second product, $C_{18}H_{16}O_7$ (**2**), was a dihydroxytrimethoxy-4-arylcoumarin, based on spectral evidence. The B ring substitution pattern was still 3′-hydroxy-4′-methoxy, as confirmed by a comparison of the ^{1}H NMR spectra with those of compounds **1** and **1a**. The second hydroxyl was placed on C-8 after consideration of the low intensity of the $[M-Me]^+$ ion in the mass spectrum and the absence of resonances at δ60 in the ^{13}C NMR spectrum of **2**. Likewise, in the ^{1}H NMR spectrum of the acetyl derivative **2a** the H-2′ and H-6′ signals were shifted downfield, whereas the H-6 proton was only slightly affected. Finally, mild treatment of **2** with diazomethane gave two products, which were coincident with **1** and **4**, thus supporting the methylation of an 8-hydroxy group and the structure 8,3′-dihydroxy-5,7,4′-trimethoxy-4-arylcoumarin for **2**.

The third 4-arylcoumarin, $C_{17}H_{14}O_7$ (**3**), possessed three hydroxyl and two methoxyl groups. One of the hydroxyl groups can be placed on C-8 because of the absence of an intense $[M-Me]^+$ ion in the mass spectrum of **3**, while the remaining hydroxyls could be located in the B ring by a comparison of the ^{1}H NMR spectra in acetone-d_6 and pyridine-d_5 (60 MHz) with those of the corresponding 5,7-dimethoxy-4-arylcoumarin **3a** [1]. The presence of two hydroxyls in the 3′ and 4′ positions cannot be strictly distinguished from the 2′,5′-dihydroxy-

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*Part 6 in the series 'Constituents of *Coutarea hexandra*'. For Part 5 see ref. [4].

substitution pattern only by the ^{1}H NMR data [3, 4]. This was confirmed by preparation of the methylenedioxy derivative **5**. Compound **5** on methylation gave **5a**, which only displayed in the ^{13}C NMR and mass spectra the typical features of an 8-methoxy group, thus confirming the presence of an 8-hydroxy group in **3**.

Examination of the UV spectra of compounds **2**, **3** and **5** revealed that the 8-hydroxy group is sensitive to the addition of sodium methoxide, but the resulting bathochromic shifts in both the absorption bands are minor compared with those observed when a 5-hydroxy group is present [4]. Notably, compounds **1**–**3** as well exostemin and its methyl ether [5] are the 8-oxygenated derivatives of the previously isolated neoflavonoids of the benzene extract of *C. hexandra* [1].

EXPERIMENTAL

General. Mps: uncorr. MS: direct inlet, 70 eV. ^{1}H and ^{13}C NMR: 300 and 75 MHz, respectively, TMS as int standard. ^{13}C NMR spectral assignments were made by comparison of chemical shifts with published data [9, 11].

Isolation. Collection and identification of plant material are reported in ref. [1]. A portion of the C_6H_6 extract by CC on silica gel with $CHCl_3$–MeOH mixts gave *inter alia* the 4-arylcoumarins described in previous papers [1, 2, 4, 5]. Compound **1** (10 mg) was obtained during the purification of exostemin [4] by prep. TLC with C_6H_6–EtOAc (4:1). Compound **2** (210 mg) was the main component of the fourth fr. eluted with $CHCl_3$–MeOH (99:1) and was purified by CC on silica gel with CH_2Cl_2–EtOAc (4:1). Compound **3** (70 mg) was isolated from the second fr. eluted with CH_2Cl_2–MeOH (19:1) and purified by CC on Sephadex LH-20 with MeOH.

3′-Hydroxy-5,7,8,4′-tetramethoxy-4-phenylcoumarin (**1**). Mp 161–162° (MeOH). UV λ_{max}^{MeOH} nm (log ε): 263 (4.18), 324 (4.09). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 1718, 1610, 1595, 1513, 1348,1280, 1244, 1109, 1060, 862. ^{1}H NMR (Me_2CO-d_6): δ 7.75 (1H, *s*, exchg D_2O, 3′-OH), 6.98 (1H, *d*, *J* = 8.2 Hz, H-5′), 6.87 (1H, *d*, *J* = 2 Hz, H-2′), 6.79 (1H, *dd*, *J* = 8.2 + 2 Hz, H-6′), 6.64 (1H, *s*, H-6), 5.87 (1H, *s*, H-3), 3.99, 3.90, 3.83 (3H each, *s*, 7-OMe, 8-OMe, 4′-OMe), 3.56 (3H, *s*, 5-OMe). ^{13}C NMR (DMSO-d_6): δ 159.3 (C-2), 155.7, 155.3 (C-4, C-7), 153.6 (C-5), 147.7 (C-4′), 145.5 (C-3′), 144.6 (C-8a), 132.0 (C-1′), 129.8 (C-8), 118.2 (C-6′), 114.9 (C-2′), 111.5, 111.2 (C-3, C-5′), 102.8 (C-4a), 94.0 (C-6), 60.7 (8-OMe), 56.3, 56.1, 55.6 (3 × OMe). EIMS *m/z* (rel. int.): 358 $[M]^+$ (100), 343 $[M-Me]^+$ (43), 330 $[M-CO]^+$ (3), 315 $[M-COMe]^+$ (18), 287 $[M-43-CO]^+$ (14), 179 $[M/2]^+$ (3), 171.5 $[M-Me/2]^+$ (3), 165 $[M-CO/2]^+$ (2), 157.5 $(M-Ac/2]^+$ (3). (Found: C, 63.80; H, 5.02; $C_{19}H_{18}O_7$ requires: C, 63.67; H, 5.07).

Acetyl derivative (**1b**). With pyridine–Ac_2O, mp 177–178° (Et_2O). ^{1}H NMR ($CDCl_3$): δ 7.14 (1H, *dd*, *J* = 2 + 8.5 Hz, H-6′), 6.98 (1H, *d*, *J* = 8.5 Hz, H-5′), 6.97 (1H, *d*, *J* = 2 Hz, H-2′), 6.29 (1H, *s*, H-6), 6.02 (1H, *s*, H-3), 3.95, 3.93, 3.89 (3H each, *s*, 3 × OMe), 3.52 (3H, *s*, 5-OMe), 2.32 (3H, *s*, Ac).

8,3′-Dihydroxy-5,7,4′-trimethoxy-4-phenylcoumarin (**2**). Mp 191–192° (MeOH). UV λ_{max}^{MeOH} nm (log ε): 271 (4.19), 324 (4.10); λ_{max}^{MeONa}: 286, 332, 384 sh; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3545, 1712, 1610, 1590, 1512, 1176, 1112, 1050, 860. ^{1}H NMR (Me_2CO-d_6): δ 7.82, 7.73 (1H each, *br s*, exchg D_2O, 8-OH, 3′-OH), 6.98 (1H, *d*, *J* = 8.2 Hz, H-5′), 6.83 (1H, *d*, *J* = 2 Hz, H-2′), 6.79 (1H, *dd*, *J* = 8.2 + 2 Hz, H-6′), 6.65 (1H, *s*, H-6), 5.85 (1H, *s*, H-3), 3.97, 3.90 (3H each, *s*, 7-OMe, 4′-OMe), 3.51 (3H, *s*, 5-OMe); δ (pyridine-d_5) -δ (Me_2CO-d_6) = H-2′ (+0.34), H-5′ (+0.02), H-6′ (+0.03), H-6 (−0.12). ^{13}C NMR (DMSO-d_6): δ160.6 (C-2), 156.26 (C-5), 151.9, 150.8 (C-7, C-8a), 148.2 (C-4′), 145.6 (C-4), 143.9 (C-3′), 133.6 (C-1′), 128.1 (C-8), 119.1 (C-6′), 115.3 (C-2′), 111.7, 111.4 (C-3, C-5′), 103.3 (C-4a), 94.5 (C-6), 56.8, 56.1 (3 × OMe). EIMS *m/z* (rel. int.): 344 $[M]^+$ (100), 329 $[M-Me]^+$ (10), 316 $[M-CO]^+$ (25), 301 $[M-Ac]^+$ (25), 297 (25), 273 $[M-43-CO]^+$ (13), 269 (23); (Found: C, 62.67; H, 4.72; $C_{18}H_{16}O_7$ requires: C, 62.77; H, 4.68).

Acetyl derivative (**2a**). With pyridine–Ac_2O; mp 220–221° (Et_2O). ^{1}H NMR ($CDCl_3$): δ 7.14 (1H, *dd*, *J* = 2 + 8.5 Hz, H-6′), 6.97 (1H, *d*, *J* = 8.5 Hz), 6.97 (1H, *d*, *J* = 2 Hz), 6.31 (1H, *s*, H-6), 6.01 (1H, *s*, H-3), 3.91, 3.89 (3H each, *s*, 7-OMe, 4′-OMe), 3.55 (3H, *s*, 5-OMe), 2.41, 2.32 (3H each, *s*, 2 × Ac).

Dimethyl derivative (**2b**). A soln of satd CH_2N_2 in Et_2O (5 ml) was added to **2** (45 mg) in MeOH (1 ml). After 15 min the reaction mixt. was evapd and the residue by CC on silica gel with $CHCl_3$ gave **2b** (40 mg).

5,7,8,3′,4′-Pentamethoxy-4-phenylcoumarin (**2b**). 220–221° sub. (Et_2O). UV λ_{max}^{MeOH} nm (log ε): 262 (4.18), 325 (4.16). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1721, 1608, 1590, 1510, 1254, 1143, 1132, 1118, 1061, 1025, 963, 912, 858, 808. ^{1}H NMR ($CDCl_3$): δ6.89 (1H, *d*, *J* = 8 Hz, H-5′), 6.86 (1H, *dd*, *J* = 1.8 + 8 Hz, H-6′), 6.81 (1H, *d*, *J* = 1.8 Hz, H-2′), 6.31 (1H, *s*, H-6), 6.04 (1H, *s*, H-3), 3.97, 3.95, 3.94, 3.87 (3H each, *s*, 4 × OMe), 3.50 (3H, *s*, 5-OMe). EIMS *m/z* (rel. int.): 372 $[M]^+$ (100), 357 $[M-Me]^+$ (71), 344 $[M-CO]^+$ (8), 329 $[M-COMe]^+$ (4), 301 $[M-43-CO]^+$ (35), 286 (16), 271 (10), 186 $[M/2]^+$ (6), 178.5 $[M-Me/2]^+$ (2), 172 $[M-CO/2]^+$ (7), 171 $[M-OMe/2]^+$ (8), 170.5 $[M-31/2]^+$ (4), 164.5 $[M-Ac/2]^+$ (9), 150.5 $[M-43-CO/2]^+$ (4). Compound **2b** was also obtained by treatment of **1** and **3** with CH_2N_2 under the same conditions.

Monomethyl derivative. To a soln of **2** (50 mg) in Et_2O (4 ml) and MeOH (few drops) a satd soln of CH_2N_2 in Et_2O (2 ml) was added. The reaction mixt. was immediately evapd and the residue by CC on silica gel with C_6H_6–EtOAc (4:1) gave 3′-hydroxy-5, 7,8,4′- tetramethoxy -4- phenylcoumarin (36 mg), which was identical with compound **1** (mmp 160–161°).

8,3′,4′-Trihydroxy-5,7-dimethoxy-4-phenylcoumarin (**3**). Mp 253–255° ($CHCl_3$–MeOH). UV, ^{1}H NMR and MS data were in agreement with those reported in ref. [5]. UV λ_{max}^{MeONa} nm: 287, 330, 386. ^{13}C NMR (DMSO-d_6): δ 161.6 (C-2), 157.1 (C-5), 150.8, 150.2 (C-7, C-8a), 144.8 (C-4), 143.5, 143.1 (C-3′, C-4′), 131.1 (C-1′), 127.6 (C-8), 119.1 (C-6′), 114.4, 113.9 (C-2′, C-5′), 111.1 (C-3), 103.4 (C-4a), 93.4 (C-6), 55.80 (2 × OMe). Found: C, 63.16; H, 4.42; Calcd for $C_{17}H_{14}O_7$: C, 63.14; H, 4.37.

Acetyl derivative (**3a**). With pyridine–Ac_2O, mp 198–200° (Et_2O). ^{1}H NMR ($CDCl_3$): δ 7.21 (1H, *d*, *J* = 8.5 Hz, H-5′), 7.14 (1H, *dd*, *J* = 2 + 8.5 Hz, H-6′), 7.09 (1H, *d*, *J* = 2 Hz, H-2′), 6.29 (1H, *s*, H-6), 6.04 (1H, *s*, H-3), 3.91 (3H, *s*, 7-OMe), 3.51 (3H, *s*, 5-OMe), 2.42, 2.33, 2.30 (3H each, *s*, 3 × Ac).

Methylenation. Compound **3** (25 mg) and dry CsF (100 mg) were shaken and cooled in dry DMF (1 ml). The suspension was added with CH_2Br_2 (0.2 ml) and maintained at 115° for 24 hr under stirring. The cooled mixt. was poured into EtOAc and washed with H_2O. The organic layer was evapd and the residue by prep. TLC on silica gel (× 2) with $CHCl_3$–MeOH (49:1) gave 8-hydroxy-5,7-dimethoxy-3′,4′-methylenedioxy -4- phenylcoumarin (**5**, 11 mg), vitreous solid: UV λ_{max}^{MeOH} nm (log ε): 271 (4.06), 322 (4.0); λ_{max}^{MeONa}: 291, 328 sh, 386 sh. ^{1}H NMR (Me_2CO-d_6): δ7.88 (1H, *br s*, exchg D_2O, 8-OH), 6.88 (1H, *d*, *J* = 8.5 Hz, H-5′), 6.84 (1H, *d*, *J* = 2 Hz, H-2′), 6.82 (1H, *dd*, *J* = 2 + 8.5 Hz, H-6′), 6.64 (1H, *s*, H-6), 6.04 (2H, *s*, OCH_2O), 5.85 (1H, *s*, H-3), 3.96 (3H, *s*, 7-OMe), 3.51 (3H, *s*, 5-OMe). EIMS *m/z* (rel. int.): 342 $[M]^+$ (100), 327 $[M-Me]^+$ (1), 314 $[M-CO]^+$ (7), 299 $[M-Ac]^+$ (12), 297 $[M-Me-OCH_2]^+$ (13), 284 $[M-CO-OCH_2]^+$ (4), 271 $[M-43-CO]^+$ (4), 269 $[M-43-OCH_2]^+$ (8), 241 [271 $-OCH_2]^+$, 171 $[M/2]^+$ (4). Methylation of **5** with CH_2N_2 gave 3′,4′-methylenedioxy-5,7,8-trimethoxy-4-phenylcoumarin (**6**, 10 mg). Mp 206–207° (Et_2O–hexane): UV λ_{max}^{MeOH} nm (log ε): 262 (4.05), 320 (3.98). ^{1}H NMR ($CDCl_3$): δ 6.83 (1H,

d, $J = 8.5$ Hz, H-5'), 6.75 (1H, *d*, $J = 2$ Hz, H-2'), 6.75 (1H, *dd*, $J = 2 + 8.5$ Hz, H-6'), 6.30 (1H, *s*, H-6), 6.02 (2H, *s*, OCH_2O), 6.0 (1H, *s*, H-3), 3.96, 3.93 (3H each, *s*, 7-OMe, 8-OMe), 3.52 (3H, *s*, 5-OMe). ^{13}C NMR ($CDCl_3$): δ 160.2 (C-2), 155.8, 155.1, 153.8 (C-7, C-5, C-4), 147.4 (C-3'), 146.8 (C-4'), 145.9 (C-8a), 133.6 (C-1'), 129.7 (C-8), 120.8 (C-6'), 108.2 (C-2'), 107.5 (C-5'), 102.3 (C-4a), 101.2 (OCH_2O), 92.7 (C-6), 61.6 (8-OMe), 56.3, 56.0 (5-OMe, 7-OMe). EIMS *m/z* (rel. int.): 356 $[M]^+$ (100), 341 $[M-Me]^+$ (50), 328 $[M-CO]^+$ (5), 326 $[M-OCH_2]^+$ (5), 313 $[M-Ac]^+$ (22), 298 $[328-OCH_2]^+$ (8), 285 $[M-43-CO]^+$ (8), 270 $[298-CO]^+$ (5), 255 $[285-OCH_2]^+$ (5), 178 $[M/2]^+$ (3).

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DIARYLPROPANES FROM *IRYANTHERA ULEI**

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Key Word Index—*Iryanthera ulei*; Myristicaceae; bark; trunk wood; dihydrochalcones; 1,3-diarylpropanes; neolignans.

Abstract—*Iryanthera ulei* (Myristicaceae) gave two dihydrochalcones, including the new 2',4'-dihydroxy-3,4,6'-trimethoxy-derivative, five diarylpropanes, including the new 1-(2',4'-dihydroxy-6'-methoxy-3',5'-dimethylphenyl)-3-(2''-hydroxy-4'',5''-methylenedioxyphenyl)-propane, and two neolignans.

INTRODUCTION

Iryanthera ulei Warb. is a tree which occurs abundantly in the Amazon region of South America where, as so many species of the Myristicaceae, it is popularly designated ucuúba. In previous studies its bark was found to contain the dihydrochalcone **1a** together with a group of lignoflavonoids, the iryantherins B, D, E and F [1]. In the present study the additional presence of the new dihydrochalcone **1b** and of two known neolignans, *trans*-burchellin [2] and *cis*-burchellin [3] is reported. The trunk wood of *I. ulei* had been found to contain (2*S*,3*R*,4*S*)-3-hydroxy-4- methyl-(19'-piperonyl-1'-*n*- nonadecyl)butanolide (juruenolide) [4]. In the present study of the same material we describe the isolation of the two dihydrochalcones **1a** and **1b**, the former having been found previously in *I. laevis*. Of the five 1,3-diarylpropanes, **2a**–**e**, **2a** and **b** have been previously isolated from *I. grandis* and *I. coriacea* [5], **2c** from *I. coriacea* [6] and **2d** from *I. laevis* [7].

RESULTS

The dihydrochalcone **1a** was identified by direct comparison with a sample of the known compound. The isolate **1b** was also classified as a dihydrochalcone. Indeed its elementary formula, $C_{18}H_{20}O_6$, determined from

*Part 33 in the series 'The Chemistry of Brazilian Myristicaceae'. For part 32 see ref. [1]. Based in part on the Doctorate thesis presented by L.M.C. to Universidade de São Paulo (1990).