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COUMARINS FROM *PARAMIGNYA MONOPHYLLA* ROOT BARK

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Key Word Index—*Paramignya monophylla*; Rutaceae; root bark; coumarins; pyranocoumarins.

Abstract—The root bark of *Paramignya monophylla* was found to contain two new coumarins, 5-methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl)pyranocoumarin and 5-hydroxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethyl octa-1,5-dien-3-yl)pyranocoumarin. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Paramignya monophylla is a woody climber growing in moderate altitudes in the dry and wet zones of Sri Lanka [1]. We have previously reported the presence of tirucalladienes in its fruits [2] and sitosterol, poncitrin (dentatin), nordentatin, 5-hydroxy- and 5-methoxy-8,8-dimethyl-10-(3,7-dimethylocta-1,6-dien-3-yl)pyranocoumarin in its stem bark [3]. The root bark contains, in addition to the stem bark constituents, xanthyletin (**1**) and two new coumarins, 5-methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethyl-octa-1,5-dien-3-yl)-2H,8H-benzo[1,2-b:5,4-b]dipyrane-2-one [5-methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl) pyranocoumarin] (**2**) and 5-hydroxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethyl-octa-1,5-dien-3-yl)-2H,8H-benzo[1,2-b:5,4-b] dipyran-2-one [5-hydroxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethyl-octa-1,5-dien-3-yl) pyranocoumarin] (**3**).

RESULTS AND DISCUSSION

The dichloromethane extract of the root bark contained poncitrin (dentatin), nordentatin, 5-hydroxy- and 5-methoxy-8,8-dimethyl-10-(3,7-dimethylocta-1,6-dien-3-yl)pyranocoumarin, sitosterol, xanthyletin (**1**) and the new coumarins (**2** and **3**).

UV spectra suggested that **2** and **3** were linear pyranocoumarins, while IR indicated that hydroxyl groups were present. Their ^{1}H NMR spectra showed them to be 5,8-disubstituted with the coumarin 3- and 4-protons and the pyran ring 6- and 7-protons appearing as two AB double doublets. A six-proton dimethyl singlet confirmed that they were dimethylpyranocoumarins. A methyl singlet at δ 3.81 and the low-field position of the H-4 doublet in the spectrum of **2** suggested that the 5-position was oxygenated with an OMe group. The hydroxyl group must therefore be on the side-chain at the 8-position, which from molecular formula considerations would have the formula, $C_{10}H_{15}O$.

The ^{1}H NMR spectrum also indicated the presence of a 1-methylallyl system. The remaining side-chain signals in the spectrum run in $CDCl_3$ were two 1H double doublets, at δ 2.59 and 2.91 for CH_2 protons, a 2H vinyl proton multiplet at δ 5.51 and a 6H methyl singlet at δ 1.11. The multiplet at δ 5.51 was resolved into two doublets, *trans*-coupled to each other (J = 15.5 Hz) when the spectrum was run in C_6D_6, suggesting that the side-chain contained an *E*-$CH_2CH{=}CHC(OH)Me_2$ moiety, probably attached to the 1-methylallyl system.

Acetylation of **2** with acetic anhydride and pyridine gave an acetate (**4**), but only at higher temperatures, as expected for a tertiary hydroxyl group. The ^{1}H NMR methyl signal of the $Me_2C(OH)$ group was shifted by 0.13 ppm on acetylation, providing further evidence for the proximity of the methyl groups to the hydroxyl group. Dehydration of **2** with *p*-toluenesulphonyl chloride gave triene **5**, while alkaline-induced cyclisation gave the *cis*-acid, **6**. The coumarin must therefore have the structure 5-methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl)-2H,8H-benzo[1,2-b:5,4-b]dipyrane-2-one.

The ^{1}H NMR spectrum of **3** was similar to that of **2**, except that the methyl singlet at δ 3.81 was absent. When **3** was methylated with CH_2N_2, **2** was obtained, indicating that **3** contained a 5-hydroxy group. Coumarin **3** must therefore be 5-hydroxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl)pyranocoumarin (**3**).

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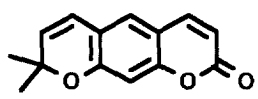

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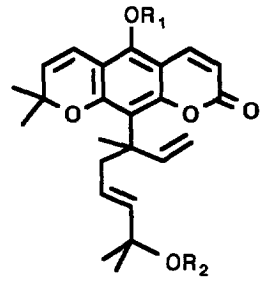

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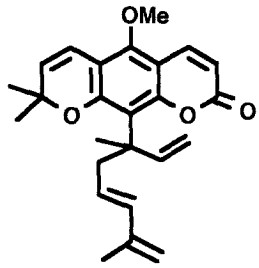
(3) R_1= R_2= H

(4) R_1=Me, R_2= OAc



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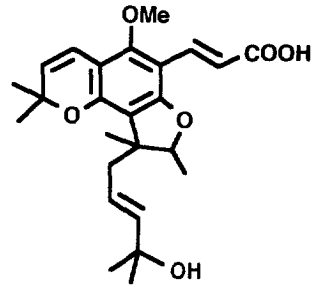

(6)

EXPERIMENTAL

UV: EtOH. IR: KBr. ^{1}H NMR: Varian 60 MHz; Brucker 200 and 400 MHz, $CDCl_3$, TMS_4 int. standard. Optical rotations: $CHCl_3$, 22°. Prep. TLC: Merck Silica Gel $PF_{254+366}$. Medium Pressure Liquid (MPLC) and Flash Chromatography (FC): Merck 9385 Kieselgel 60 (230–400 mesh ASTM). Identities of compounds were established by mmp, IR and ^{1}H NMR comparisons, unless stated otherwise.

Paramignya monophylla Wight was collected from Hewaheta in the Kandy district in central Sri Lanka and identified by the late Prof. S. Balasubramaniam of the Department of Botany of the University. Voucher specimen No. 5/468B is deposited in the University Herbarium.

Extraction

Dried ground root bark (1.8 kg) was extracted successively in the cold with CH_2Cl_2 for two 24 h periods. Concn. of the CH_2Cl_2 solns gave 30 g of extract.

Chromatography of CH_2Cl_2 *extract*

The extract (25 g) on silica gel (125 g) was subjected to MPLC on silica gel (210 g). Elution with hexane–EtOAc (4:1), followed by FC with CH_2Cl_2–hexane (7:3), gave 5-methoxy-8,8-dimethyl-10-(3,7-dimethylocta-1,6-dien-3yl)pyranocoumarin as an oil (1.2 g), $[\alpha]_D$ +12.0° and poncitrin (2.1 g) as pale yellow needles from CH_2Cl_2–hexane, mp 92° (lit. [3] mp 92°), while elution with EtOAc–hexane (4:21), after similar FC, gave sitosterol (30 mg) mp 138° (lit. [4] mp 137°), identical with authentic materials. Elution with hexane–EtOAc (2:3) gave a pale yellow gum which on FC [EtOAc–hexane (7:13)] yielded prisms of xanthyletin (**1**) (30 mg), mp 154° (lit. [4] mp. 153°–154°) and a fr., which on FC with CH_2Cl_2–MeOH (97:3) and prep. TLC [CH_2Cl_2–MeOH (97:3)], gave 5-hydroxy-8,8-dimethyl-10-(3,7-dimethylocta-1,6-dien-3yl)pyranocoumarin, as a yellow oil (200 mg), $[\alpha]_D$ +29°, and nordentatin (40 mg), mp 183° (lit. [3] mp 183°), identical with authentic materials.

Elution with EtOAc–hexane (4:1) gave an oil (2.0 g) which on FC [silica gel (40 g)] using CH_2Cl_2–MeOH (44:1), gave 5-methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl)-2H,8H-benzo[1,2-b:5,4-b]dipyrane-2-one (**2**) as a yellow oil (1.1 g), $[\alpha]_D$ −3.9° (*c* 0.1). (Found: C, 73.1, H, 7.3; $C_{25}H_{30}O_5$ requires C, 73.1, H, 7.4); UV λ_{max} nm (log ε): 207 (4.12), 228 (4.24), 270 (4.31) 327 (1.22). IR ν_{max} cm^{-1}: 3400, 2900, 1720, 1600, 1500. ^{1}H NMR (400 MHz): δ 1.11 (6H, *s*, 7′-Me and 8′-H), 1.43 and 1.46 (each 3H,

s, 8-Me), 1.69 (3H, *s*, 3′-Me), 2.59 (1H, *dd*, J = 13.4 and 6 Hz, 4′-H), 2.91 (1H, *dd*, J = 13.4 and 5.2 Hz, 4′-H), 3.81 (3H, *s*, 5-OMe), 4.90 (1H, *dd*, J = 10.7 and 1.0 Hz, 1′-H), 4.95 (1H, *dd*, J = 17.5 and 1.0 Hz, 1′-H), 5.51 (2H, *m*, 5′- and 6′-H), 5.68 (1H, *d*, J = 9.9 Hz, 7-H), 6.17 (1H, *d*, J = 9.6 Hz, 3-H), 6.36 (1H, *dd*, J = 17.4 and 10.7 Hz, 2′-H), 6.55 (1H, *d*, J = 9.9 Hz, 6-H) and 7.86 (1H, *d*, J = 9.6 Hz, 4-H); ^{1}H NMR (400 MHz, C_6D_6): 1.11 and 1.13 (each 3H, *s*, 7′-Me and 8′-H), 1.25 (6H, *s*, 8-Me), 1.90 (3H, *s*, 3′-Me), 2.79 (1H, *ddd*, J = 13.5, 7.1 and 1.0 Hz, 4′-H), 3.17 (1H, *ddd*, J = 13.5, 7.2 and 1.1 Hz, 4′-H), 3.28 (3H, *s*, 5-OMe), 5.03 (1H, *dd*, J = 10.7 and 1.0 Hz, 1′-H), 5.09 (1H, *dd*, J = 17.5 and 1.1 Hz, 1′-H), 5.29 (1H, *d*, J = 9.9 Hz, 7-H), 5.62 (1H, *dt*, J = 15.5 and 1.0 Hz, 6′-H), 5.74 (1H, *dt*, J = 15.5 and 7.2 Hz, 5′-H), 5.92 (1H, *d*, J = 9.6 Hz, 3-H), 6.48 (1H, *d*, J = 9.9 Hz, 6-H), 6.57 (1H, *dd*, J = 17.5 and 10.7 Hz, 2′-H), 7.32 (1H, *d*, J = 9.6 Hz, 4-H). ^{13}C NMR (C_6D_6): δ 27.4 and 27.5 (7′-Me and 8′-C), 28.4 (3′-Me), 29.9 and 30.0 (8-Me), 43.1 (4′-C), 45.3 (3′-C), 62.8 (5-OMe), 70.1 (7′-C), 77.3 (8-C), 107.7 (4a-C), 108.6 (1′-C), 111.6 (5a-C), 112.2 (3-C), 116.7 (6-C), 118.0 (10-C), 123.6 (5′-C), 129.6 (7-C), 138.2 (4-C), 141.6 (6′-C), 149.7 (2′-C), 151.8 (5-C), 155.1 (10a-C), 156.2 (9a-C), 159.6 (C=O). MS *m/z* (rel. int.): 410 $[M]^+$ (0.3), 371 (1.5), 311 (100), 281 (38), 271 (10), 253 (8).

Further elution with EtOAc–Hexane (6:1) gave a brown gum (300 mg), which on FC on silica gel (30 g) with EtOAC–hexane (6.5:1) gave **3** as a yellow semi-solid (44 mg), $[\alpha]_D$ −5.45° (*c* 1.1). HRMS: *m/z* 378.1831 $[M-H_2O]^+$. Calcd for $C_{24}H_{26}O_4$: 378.1831. UV λ_{max} nm (log ε): 229 (4.10), 283 (4.00), 340 (4.19). IR ν_{max} cm^{-1}: 3400, 2900, 1720, 1590, 1470. ^{1}H NMR (60 MHz): δ 1.13 (6H, *s*, 7′-Me and 8′-H), 1.41 (6H, *s*, 8-Me), 1.64 (3H, *s*, 3′-Me), 2.64 (2H, *m*, 4′-H), 4.83 (1H, *d*, J = 11 Hz, 1′-H), 4.86 (1H, *d*, J = 18 Hz, 1′-H), 5.50 (2H, *m*, 5′- and 6′-H), 5.55 (1H, *d*, J = 10 Hz, 7-H), 5.98 (1H, *d*, J = 9.5 Hz, 3-H), 6.28 (1H, *dd*, J = 18 and 11 Hz, 2′-H), 6.54 (1H, *d*, J = 10 Hz, 6-H), 7.95 (1H, *d*, J = 9.5 Hz, 4-H). ^{13}C NMR (50 MHz): 27.2 and 27.3 (7′-Me and 8′-C), 27.8 (3′-C), 29.6 (8-Me), 43.4 (4′-C), 45.3 (3′-C), 70.6 (7′-C), 77.3 (8-C), 107.8 (4a-C), 110.7 (1′-C), 112.2 (3a-C), 115.5 (5a-C), 118.9 (6-C), 121.3 (10-C), 123.6 (5′-C), 130.0 (7-C), 138.8 (4-C), 141.4 (6′-C), 148.6 (2′-C), 152.5 (5-C), 155.1 (10a-C), 156.6 (9a-C), 159.4 (C=O). MS *m/z* (rel. int.): 378 $[M-H_2O]^+$ (20), 363 (40), 297 (100), 295 (22), 281 (21), 229 (16) and 125 (22).

5-*Methoxy*-8,8-*dimethyl*-10-(7-*acetoxy*-3,7-*dimethyl*-*octa*-1,5-*dien*-3-*yl*)-2*H*,8*H*-*benzo*[1,2-*b*:5,4-*b*]*dipyran*-2-*one* (**4**). The coumarin (**2**) (100 mg) in dry pyridine (1 ml) was refluxed with Ac_2O (1 ml) at 110° for 24 h. Work-up, followed by prep TLC (CH_2Cl_2), gave **4** as a colourless oil (50 mg). $[\alpha]_D$ −1.7°. HRMS: 452.2199 $[M]^+$. Calcd for $C_{27}H_{32}O_6$: 452.2199. IR ν_{max} cm^{-1}: 3000, 1730, 1720, 1610, 1570, 1440, 1240. ^{1}H NMR (60 MHz): δ 1.31 and 1.34 (each 3H, *s*, 7′-Me and 8′-H), 1.48 (6H, *bs*, 8-Me), 1.73 (3H, *s*, 3′-Me), 1.86 (3H, *s*, -OAc), 2.4–3.2 (2H, *m*, $w_{1/2}$ = 15 Hz, 4′-H), 3.84 (3H, *s*, 5-OMe), 4.93 (1H, *dd*, J = 10.5 and 1 Hz, 1′-H), 4.95 (1H, *dd*, J = 17 and 1 Hz, 1′-H), 5.49 and 5.52 (each 1H, *m*, $w_{1/2}$ = 12 and 6 Hz, 5′- and 6′-H), 5.71 (1H, *d*, J = 9.5 Hz, 7-H), 6.19 (1H, *d*, J = 9.6 Hz, 3-H), 6.40 (1H, *dd*, J = 17 and 10.5 Hz, 2′-H), 6.60 (1H, *d*, J = 9.5 Hz, 6-H), 7.90 (1H, *d*, J = 9.6 Hz, 4-H). MS *m/z* (rel. int.): 452 $[M]^+$ (9), 437 (5), 392 (25), 377 (27), 349 (16), 311 (100), 297 (30), 281 (35), 271 (19).

5-*Methoxy*-8,8-*dimethyl*-10-(3,7-*dimethyl*-1,5,7-*trien*-3*yl*)-2*H*,8*H*-*benzo*[1,2-*b*:5,4-*b*]*dipyran*-2 *one* (**5**). Coumarin (**2**) (50 mg) in dry pyridine (2 ml), *p*-TsCl (25 mg) and dimethylaminopyridine (4 drops) were refluxed at 125° for 15 h, worked-up with CH_2Cl_2 and purified by FC with EtOAc–hexane (3:7) to give **5** as an oil (15 mg). HRMS: 392.1986 $[M]^+$. Calcd for $C_{25}H_{28}O_4$: 392.1988. $[\alpha]_D$ −2.9° (*c* 0.7). UV: λ_{max} (nm, log ε): 213 (4.27), 271 (4.11), 327 (3.93). IR ν_{max} (cm^{-1}): 3000, 1710, 1610, 1750, 1440, 1240, 1150. ^{1}H NMR (60 MHz): δ 1.40 and 1.45 (each 3H, *s*, 8-Me), 1.68 (6H, *bs*, 3′-and 7′-Me), 2.63 and 2.90 (each, 1H, *dd*, J = 13.5 and 7 Hz, 4′-H), 3.76 (3H, *s*, 5-OMe), 4.72 (2H, *m*, $w_{1/2}$ = 3 Hz, 8′-H), 4.84 (1H, *dd*, J = 11 and 1 Hz, 1′-H), 4.87 (1H, *dd*, J = 15 and 1 Hz, 1′-H), 5.43 (1H, *d*, J = 17 Hz, 6′-H), 5.58 (1H, *d*, J = 10 Hz, 7-H), 6.08 (1H, *d*, J = 9.5 Hz, 3H), 6.10 (1H, *dt*, J = 17 and 7 Hz, 5′-H), 6.16 (1H, *dd*, J = 11 and 20 Hz, 2′-H), 6.48 (1H, *d*, J = 10 Hz, 6-H) and 7.72 (1H, *d*, J = 9.5 Hz, 4-H); MS *m/z* (rel. int.): 392 [M^+] (7), 377 (10), 311 (100), 281 (32), 253 (13).

6-(3-*Carboxyethenyl*)-5-*methoxy*-2,2,8,9-*tetra*-*methyl*-9-(4′-*methyl*-4′-*hydroxypent*-3′-*enyl*)-2*H*-*furo*[2,3-*h*]*chromene* (**6**). Coumarin (**2**) (138 mg) in MeOH (6 ml) was stirred with aq. NaOH (20%, 3 ml) at 25° for 12 h. Neutralisation (2 N HCl), followed by work-up, gave a crude product, which on FC with CH_2Cl_2:MeOH (49:1) gave **6** (180 mg) as yellow cystals from CH_2Cl_2–hexane, mp 74°. $[\alpha]_D$ −16.1° (*c* 0.6). (HRMS: 428.2197 $[M]^+$. Calcd for $C_{25}H_{32}O_6$: 428.2199). UV: λ_{max} nm (log ε): 284 (3.45), 271 (3.50), 222 (4.22). IR: ν_{max} cm^{-1}: 3000, 1700, 1610, 1590, 1440, 1220, 1120. ^{1}H NMR (60 MHz): δ 1.16 (3H, *s*, 9-Me), 1.20 (3H, *d*, J = 7 Hz, 8-Me), 1.26 (6H, *s*, 4′-Me and 5′-H), 1.41 (6H, *s*, 2-Me), 2-2.9 (2H, *m*, 1′-H), 3.68 (3H, *s*, 5-OMe), 4.60 (1H, *q*, J = 7 Hz, 8-H), 5.40 (1H, *d*, J = 9.5 Hz, 7-H), 5.46 (1H, *d*, J = 9 Hz, 3-H), 5.57 (2H, *m*, $w_{1/2}$ = 4 Hz, 2′-H, 3′-H), 5.95 (1H, *d*, J = 12 Hz, 2′-H), 6.86 (1H, *d*, J = 12 Hz, 1′-H). MS *m/z* (rel. int.): 428 $[M]^+$ (11), 413 (15), 395 (5), 329 (100), 299 (24), 285 (50), 269 (30), 239 (30).

Methylation of **3**. Coumarin **3** (24 mg) on stirring with excess CH_2N_2–Et_2O at 25° for 2 h. gave **2** (20 mg), identical with that isolated above.

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REFERENCES

1. *A Revised Handbook to the Flora of Ceylon*, Vol. V, ed. M. D. Dassanayake and F. R. Fosberg. Amerind, New Delhi, 1985.
2. Kumar, V., Niyaz, N. M., Wickramaratne, D. B. M. and Balasubramaniam, S., *Phytochemistry*, 1991, **30**, 1231.
3. Kumar, V., Niyaz, N. M. and Wickramaratne, D. B. M., *Phytochemistry*, 1995, **38**, 805.
4. *Dictionary of Organic Compounds*, ed. I. M. Heilbron and H. M. Bunbury. Eyre and Spottiswoode, London, 1965.