

COUMARINS FROM STEM BARK OF *PARAMIGNYA MONOPHYLLA*

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

**Abstract**—The stem bark of *Paramignya monophylla* contained poncitrin, nordinatatin, sitosterol and the new 5-hydroxy- and 5-methoxy-8,8-dimethyl-10-(3',7'-dimethylocta-1',6'-dien-3'-yl)-2H,8H-benzo[1,2-b:5,4-b']dipyran-2-one.

## INTRODUCTION

*Paramignya monophylla* is a woody climber growing in moderate altitudes in the dry and wet zones of Sri Lanka [1]. The only work on this genus is our report [2] on the presence of tirucalladienes in its fruit. The dichloromethane extract of its stem bark showed moderate anti-fungal activity against *Cladosporium cladosporoides* in the TLC-bioassay [3]. It contained sitosterol, poncitrin (dentatin) (1), nordinatatin (2) and two new coumarins, 5-hydroxy-8,8-dimethyl-10-(3',7'-dimethylocta-1',6'-dien-3'-yl)-2H,8H-benzo[1,2-b:5,4-b']dipyran-2-one] [5-hydroxy-8,8-dimethyl-10-(3',7'-dimethylocta-1',6'-dien-3'-yl)pyranocoumarin]

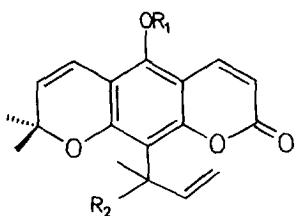
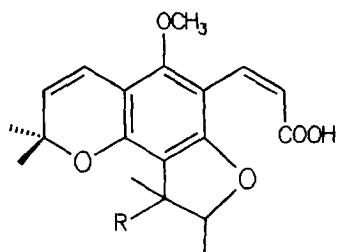
coumarin] (3) and 5-methoxy-8,8-dimethyl-10-(3',7'-dimethylocta-1',6'-dien-3'-yl)pyranocoumarin (4).

## RESULTS AND DISCUSSION

The dichloromethane extract of the stem bark of *P. monophylla* contained poncitrin (dentatin) (1), nordinatatin (2) [4, 5], sitosterol and two new coumarins. The UV spectra of the new coumarins (3 and 4) were similar to that of 1, suggesting that they were linear pyranocoumarins.

The new coumarins (3 and 4),  $C_{24}H_{28}O_4$  and  $C_{25}H_{30}O_4$ , were optically active gums. The IR spectrum of the more polar coumarin 3 showed a peak at  $3400\text{ cm}^{-1}$  indicating that a hydroxyl group was present. The  $^1\text{H NMR}$  spectra of 3 and 4 contained four doublets constituting two AB systems and the six proton singlet typical of dimethylpyranocoumarins. The low field nature of the H-4 doublet, a broad singlet at  $\delta 8.05$  in 3 and a methyl singlet at  $\delta 3.85$  in 4 suggested that they contained a hydroxy and a methoxy group at C-5, respectively. Both dimethylpyranocoumarins must contain a  $C_{10}$ -alkyl substituent at C-8. A methyl singlet and the  $\text{CH}=\text{CH}_2$  protons at  $\delta \sim 6.4$  and  $\delta \sim 4.9$  suggested that a 1-methylallyl system was present, while two vinyl methyls and multiplets at  $\delta \sim 5.1$  and  $\delta \sim 2.25$  suggested a  $\text{Me}_2\text{C}=\text{CHCH}_2$  system. A 2H multiplet at  $\delta \sim 1.9$  was assigned to an additional methylene group.

The side chain must be joined to the coumarin ring at the allyl carbon atom of the 1-methylallyl system, which must also be attached to the isopentenyl group via the additional methylene group. The appearance of base peaks at  $m/z$  297 and 311 [ $M - 83$ ]<sup>+</sup> in the mass spectra of 3 and 4, respectively, due to the loss of the  $\text{Me}_2\text{C}=\text{CH}(\text{CH}_2)_2$  was further evidence for this arrangement. Coumarins 3 and 4 should have a 3,7-dimethylocta-1,6-dien-3-yl side chain and must respectively be 5-hydroxy- and 5-methoxy-8,8-dimethyl-10-(3',7'-dimethylocta-1',6'-dien-3'-yl)-2H,8H-benzo[1,2-b:5,4-b']dipyran-2-one.

1.  $R_1 = \text{CH}_3$ ,  $R_2 = \text{CH}_3$ , Poncitrin2.  $R_1 = \text{H}$ ,  $R_2 = \text{CH}_3$ , Nordinatatin3.  $R_1 = \text{H}$ ,  $R_2 = (\text{CH}_2)_2\text{CH}=\text{CMe}_2$ 4.  $R_1 = \text{CH}_3$ ,  $R_2 = (\text{CH}_2)_2\text{CH}=\text{CMe}_2$ 5.  $R = (\text{CH}_2)_2\text{CH}=\text{CMe}_2$ 6.  $R = \text{CH}_3$

The position of the side-chain was confirmed by the alkaline induced cyclization of **4**. The spectra of the product **5** were similar to those reported for cycloponcirinic acid (**6**), formed from similar cyclization of **1**, except for the presence of signals for a  $\text{Me}_2\text{C}=\text{CH}(\text{CH}_2)_2$  moiety instead of a methyl group in its  $^1\text{H}$  NMR spectrum. Methylation of **3** with diazomethane gave **4** confirming their interrelationship.

## EXPERIMENTAL

UV: EtOH; IR: KBr;  $^1\text{H}$  NMR: Varian 60 MHz and Bruker 200 MHz,  $\text{CDCl}_3$ , TMS as int. standard; optical rotations:  $\text{CHCl}_3$ ,  $22^\circ$ ; prep. TLC: Merck silica gel  $\text{PF}_{254+366}$ ; medium pressure liquid (MPLC) and flash chromatography (FC): Merck Kieselgel 9385. Identities of compounds were established by mmp, IR and  $^1\text{H}$  NMR comparisons unless otherwise stated.

*Paramignya monophylla* was collected from Hewaheta in the Kandy district in central Sri Lanka and a voucher specimen has been deposited in the University Herbarium.

*Extraction.* The dried ground stem bark (360 g) of *P. monophylla* was successively extracted in the cold with  $\text{CH}_2\text{Cl}_2$  for two 24 hr periods each. Concn of the  $\text{CH}_2\text{Cl}_2$  solns gave 9.0 g of extract.

*Chromatography of the  $\text{CH}_2\text{Cl}_2$  extract of the stem bark.* The extract (6.5 g) on silica gel (50g) was subjected to MPLC on silica gel (70 g). Elution with EtOAc-hexane (1:49) gave an oil (680 mg), which on FC on silica gel (40 g) using  $\text{CH}_2\text{Cl}_2$ -hexane (7:3) gave **4** as a pale yellow oil (60 mg),  $[\alpha]_D + 12.7^\circ$  (*c* 0.5). (Found: C, 76.1, H, 7.8;  $\text{C}_{25}\text{H}_{30}\text{O}_4$  requires C, 76.1, H, 7.7) (HRMS: 394.2140 [M] $^+$ , Calc. for  $\text{C}_{25}\text{H}_{30}\text{O}_4$ : 394.2144); UV  $\lambda_{\text{max}}$  nm ( $\log \epsilon$ ): 207 (4.43), 228 (4.36), 272 (4.33) and 346 (4.14); IR  $\nu_{\text{max}}$  cm $^{-1}$ : 2850, 1730, 1600, 1590 and 1140;  $^1\text{H}$  NMR (200 MHz):  $\delta$  1.27 (3H, *s*, 3'-Me), 1.45 and 1.48 (each 3H, *s*, 8-Me), 1.62 and 1.73 (each 3H, *s*, 7'-Me and H-8'), 1.89 (2H, *m*, H-4'), 2.27 (2H, *m*, H-5'), 3.85 (3H, *s*, OMe), 4.90 (2H, *m*, H-1'), 5.06 (1H, *m*, H-6'), 5.71 (1H, *d*, *J* = 9.9 Hz, H-7), 6.21 (1H, *d*, *J* = 9.6 Hz, H-3), 6.38 (1H, *dd*, *J* = 12.5 and 10.7 Hz, H-2'), 6.59 (1H, *d*, *J* = 9.9 Hz, H-6) and 7.89 (1H, *d*, *J* = 9.6 Hz, H-4); MS  $m/z$  (rel. int.): 394 [M] $^+$  (17), 379 (59), 351 (14), 326 (13), 311 (100), 297 (51), 285 (29) and 242 (68).

Elution with EtOAc-hexane (1:49 and 1:9) gave respectively, poncirin (**1**) (90 mg), pale yellow needles from  $\text{CH}_2\text{Cl}_2$ -hexane, mp  $92^\circ$  (lit. [4] mp  $93\text{--}94^\circ$ ), whose spectral data were identical with those reported, and sitosterol (30 mg), mp  $138^\circ$  (lit. [6] mp  $137^\circ$ ), identical with authentic material.

Futher elution with EtOAc-hexane (1:4) gave a gum (800 mg), which on FC on silica gel (40 g) with  $\text{CH}_2\text{Cl}_2$ -hexane (7:3) and prep. TLC [ $\text{CH}_2\text{Cl}_2$ -MeOH (97:3)] gave **3** as a pale yellow oil (80 mg),  $[\alpha]_D + 2.9^\circ$  (*c* 0.5). (Found: C, 76.1, H, 7.9;  $\text{C}_{24}\text{H}_{28}\text{O}_4$  requires C, 76.1, H, 7.6); UV  $\lambda_{\text{max}}$  nm ( $\log \epsilon$ ): 207 (4.24), 277 (4.19), 278 (4.30) and

345 (4.04); IR  $\nu_{\text{max}}$  cm $^{-1}$ : 3400, 2800, 1700, 1600 and 1140;  $^1\text{H}$  NMR (200 MHz):  $\delta$  1.25 (3H, *s*, 3'-Me), 1.45 and 1.47 (each 3H, *s*, 8-Me), 1.62 and 1.72 (each 3H, *s*, 7'-Me and H-8'), 1.90 (2H, *m*, H-4'), 2.25 (2H, *m*, H-5'), 4.95 (2H, *m*, H-1'), 5.10 (1H, *m*, H-6'), 5.75 (1H, *d*, *J* = 9.9 Hz, H-7), 6.20 (1H, *d*, *J* = 9.8 Hz, H-3), 6.40 (1H, *dd*, *J* = 12.5 and 10.3 Hz, H-2'), 6.55 (1H, *d*, *J* = 9.9 Hz, H-6) and 8.05 (1H, *d*, *J* = 9.8 Hz, H-4); MS  $m/z$  (rel. int.): 380 [M] $^+$  (17), 365 (40), 337 (14), 311 (15), 297 (100), 283 (31), 255 (29) and 229 (68), and nordentatin (**2**) (80 mg), needles from  $\text{CH}_2\text{Cl}_2$ -hexane, mp  $183^\circ$  (lit. [4] mp  $182^\circ$ ), whose spectral data were identical with those reported.

*Methylation of **3**.* Coumarin **3** (70 mg) on stirring with excess ethereal  $\text{CH}_2\text{N}_2$  at  $25^\circ$  for 1 hr gave **4** (52 mg) identical with that obtained above.

6-(3'-Carboxyethenyl)-5-methoxy-2,2,8,9-tetramethyl-9-(4'-methylpent-3"-enyl)-2H-furo[2,3-h]chromene (**5**). Coumarin (**3**) (46 mg) in MeOH (2 ml) was stirred with 20% aq. NaOH (2 ml) at  $25^\circ$  for 12 hr. Neutralization (2M HCl), extraction with  $\text{CH}_2\text{Cl}_2$  and FC gave **5** (28 mg) as an oil,  $[\alpha]_D - 4.2^\circ$ . (Found: C, 72.5, H, 7.9;  $\text{C}_{25}\text{H}_{32}\text{O}_5$  requires C, 72.8, H, 7.8); UV  $\lambda_{\text{max}}$  nm ( $\log \epsilon$ ): 284 (3.45), 271 (3.50) and 222 (4.22); IR  $\nu_{\text{max}}$  cm $^{-1}$ : 3000, 1700, 1610, 1590, 1220, and 1120;  $^1\text{H}$  NMR (60 MHz):  $\delta$  1.15 (3H, *s*, 9-Me), 1.31 (3H, *d*, *J* = 6 Hz, 8-Me), 1.40 (6H, *s*, 2-Me), 1.53 and 1.63 (each 3H, *s*, 4"-Me and H-5'), 1.80 (2H, *m*, H-1''), 2.00 (2H, *m*, H-2'), 3.70 (3H, *s*, OMe), 4.60 (1H, *qt*, *J* = 6 Hz, H-8), 5.16 (1H, *m*, H-3''), 5.45 (1H, *d*, *J* = 10 Hz, H-3), 5.95 (1H, *d*, *J* = 12 Hz, H-2'), 6.56 (1H, *d*, *J* = 10 Hz, H-4) and 6.90 (1H, *d*, *J* = 12 Hz, H-1'); MS  $m/z$  (rel. int.): 412 [M] $^+$  (25), 397 (100), 329 (43), 297 (11) and 287 (15).

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## REFERENCES

- Dassanayake, M. D. and Fosberg, F. R. (eds) (1985) *A Revised Handbook to the Flora of Ceylon*, Vol. V, p. 466. Amerind, New Delhi.
- Kumar, V., Niyaz, N. M. M., Wickramaratne, D. B. M. and Balasubramaniam, S. (1991) *Phytochemistry* **30**, 1231.
- Karman, W. L. and Stanford, J. B. (1986) *Life Science* **7**, 1095.
- Govindachari, T. R., Pai, B. R., Subramaniam, P. S. and Muthukumaraswamy, N. (1968) *Tetrahedron* **24**, 753.
- Tomimatsu, T., Hashimoto, M., Shingu, T. and Tori, K. (1972) *Tetrahedron* **28**, 2003.
- Heilbron, I. M. and Bunbury, H. M. (eds) (1965) *Dictionary of Organic Compounds*. Eyre and Spottiswoode, London.