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TWO NAPHTHOPYRAN DERIVATIVES FROM *FARAMEA CYANEA**

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Key Word Index—*Faramea cyanea*; Rubiaceae; naphthopyrans; anthraquinones; lichexanthone.

Abstract—Four anthraquinones and two new products, faramol (3,4-dihydro-3-hydroxy-2,2-dimethyl-2H-naphtho[1,2-b]pyran) and 7-methoxyfaramol (3,4-dihydro-3-hydroxy-7-methoxy-2,2-dimethyl-2H-naphtho[1,2-b]pyran), have been isolated from *Faramea cyanea*.

INTRODUCTION

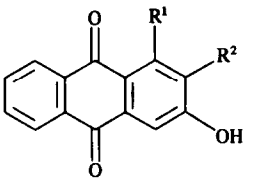
Rubiaceae are known as a source of anthraquinones and compounds with naphthalene nuclei. In the present article, we describe the isolation from *Faramea cyanea* of a xanthone, four known anthraquinones and two new naphthopyrans with a hydroxy group in the pyran ring, faramol and 7-methoxyfaramol. Faramol showed a low cytotoxicity on KB cells *in vitro* whereas it was inactive against bacteria and fungi.

RESULTS AND DISCUSSION

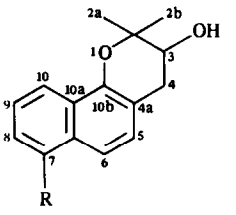
The benzene extract of the bark of *F. cyanea* afforded as main component 1-hydroxy-3,6-methoxy-8-methyl-xanthone, namely lichexanthone. Mp and physical data of lichexanthone and its acetylderivative were coincident with those of the compounds previously described from *Aspidosperma formosanum* (Apocynaceae) [1]. It was suspected [1] that the compound had come from a lichen present on the bark.

The benzene extract of the heartwood of *F. cyanea* afforded β-sitosterol, the anthraquinones **1**–**4**, faramol (**8**) and 7-methoxyfaramol (**9**). Rubiadin (**1**), 3-hydroxy-2-methylanthraquinone (**2**), 3-hydroxy-1-methoxy-2-methoxymethylanthraquinone (damnacanthol-ω-methyl ether) (**3**) and 1,3-dihydroxy-2-methoxymethylanthraquinone (lucidin-ω-methyl ether (**4**) were identified from spectral and analytical data. Compounds **3** and **4**, previously found in *Morinda lucida* [2] and *Galium album* [3] respectively, may be artefacts formed from damnacanthol and lucidin by contact with methanol.

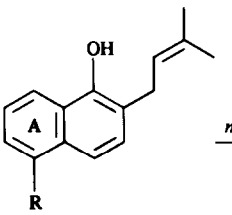
The ^{1}H NMR spectrum of the first new compound, $C_{15}H_{16}O_2$, $[M]^+$ at *m/z* 228, showed signals for six aromatic protons two of which were *ortho* coupled, whereas the remaining four disclosed an unsubstituted naphthalene ring; the resonances of two methyl groups (δ1.32 and 1.40, respectively) and of an AXY system were also present. The *A* proton (triplet at δ3.83) was shifted downfield by acetylation (δ5.03). The mass fragmentation pattern (losses of H_2O, C_4H_7O and C_4H_8O from the molecular ion) suggested the presence of a pyranol ring



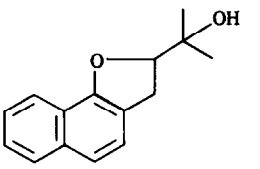
	R^1	R^2
1	OH	Me
2	H	Me
3	OMe	CH_2OMe
4	OH	CH_2OMe



8 R = H
9 R = OMe



5 R = H
6 R = OMe



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and on consideration of naphthopyrans previously isolated from Rubiaceae [4–6], structure **8** was considered the most likely. Moreover, comparison of the ^{13}C NMR spectrum with those of substituted naphthalenes [7, 8] led to a consistent assignment of the signals (Table 1). Structure **8** was confirmed by synthesis [9] from 1-hydroxy-2-prenylnaphthalene **5**. The second compound, $C_{16}H_{18}O_3$, $[M]^+$ at *m/z* 258, showed a close similarity with **8**, but an additional methoxy group in the ring A was indicated by the ^1H NMR spectrum. The pattern of the ring A protons was coincident with that of the protons of 1,5-dimethoxynaphthalene thus indicating a 7-substitution in compound **9**. In the ^{13}C NMR spectrum (Table 1) two further signals were observed in the narrow range at 114–115 ppm in addition to the one due to C-4 and were attributed to C-6 and C-10.

Comparison with model compounds [7, 8] showed that only a C-7 methoxyl group would give such an effect. The structure **9** which followed from the above considerations was also confirmed by synthesis from 1-hydroxy-5-methoxy-2-prenylnaphthalene (**6**).

EXPERIMENTAL

^1H NMR: 60 MHz with TMS as int. standard; ^{13}C NMR (Varian XL 100 Fourier transform spectrometer): 25.2 MHz; TLC and CC: Kieselgel 60 (Merck).

Plant material. Faramea cyanea Muell. Arg. was collected in Pacatuba, Ceará State, Brazil and was identified by Dr. J. Elias de Paula. A voucher sample (1384-IBGE) is deposited in the Herbarium of Centro Chimica Recettori del C.N.R.

(±)-*Faramol* (**8**). Mp 124–126° (EtOAc–*n*-hexane), $[\alpha]_D^{23} = 0°$ (MeOH); ^1H NMR ($CDCl_3$): δ1.32 (3H, *s*, Me), 1.40 (3H, *s*, Me), 2.55–3.40 (2H, *m*, CH_2-4), 3.83 (1H, *t*, *J* = 5.0 Hz, H-3), 7.07 (1H, *d*, *J* = 8.0 Hz, H-5), 7.35 (1H, *d*, *J* = 8.0 Hz, H-6), 7.30–7.55 (2H, *m*, H-8, H-9), 7.55–7.85 (1H, *m*, H-7), 8.10–8.30 (1H, *m*, H-10); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 2990, 2930, 1600, 1575, 1460, 1390, 1370, 1270, 1190, 1150, 1140, 1090, 1060, 945, 800; EIMS *m/z* (rel. int.): 228 $[M]^+$ (50), 210 $[M-H_2O]^+$ (5), 195 $[M-H_2O-Me]^+$ (30), 170 (15), 157 $[M-C_4H_7O]^+$ (100), 156 $[M-C_4H_8O]^+$ (15), 129 (30), 128 (30); ^{13}C NMR: see Table 1. Calc. for $C_{15}H_{16}O_2$: C, 78.92; N, 7.06. Found: C, 78.78, H, 6.98%. *Acetate.* Oil; ^1H NMR (CCl_4): δ1.33 (6H, *s*, 2 Me), 1.97 (3H, *s*, OAc), 2.55–3.40 (2H, *m*, CH_2-4), 5.03 (1H, *t*, *J* = 5.0 Hz, H-3), 7.00 (1H, *d*, *J* = 8.0 Hz, H-5), 7.35 (1H, *d*, *J* = 8.0 Hz, H-6), 7.30–7.80 (3H, *m*, H-7, H-8, H-9), 8.05–8.30 (1H, *m*, H-10); EIMS *m/z* (rel. int.): 270 $[M]^+$ (30), 210 $[M-AcOH]^+$ (30), 195 $[M-AcOH-Me]^+$ (100), 172 (15), 171 (25), 170 (35), 157 (80), 156 (20), 129 (25), 128 (35).

(±)-*7-Methoxyfaramol* (**9**). Mp 274–276° (Me_2CO), $[\alpha]_D^{23} = 0°$ (MeOH); ^1H NMR (60 MHz, $CDCl_3$): δ1.32 (3H, *s*, Me), 1.40 (3H, *s*, Me), 2.55–3.40 (2H, *m*, CH_2-4), 3.83 (1H, *t*, *J* = 5.0 Hz, H-3), 6.77 (1H, *dd*, *J* = 7.5, 1.0 Hz, H-8), 7.10 (1H, *d*, *J* = 8.0 Hz, H-5), 7.33 (1H, *t*, *J* = 7.5 Hz, H-9), 7.77 (1H, *d*, *J* = 8.0 Hz, H-6), 7.80 (1H, *dd*, *J* = 7.5, 1.0 Hz, H-10), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 2930, 1600, 1510, 1460, 1450, 1400, 1260, 1135, 1070, 950; EIMS *m/z* (rel. int.): 258 $[M]^+$ (50), 240 $[M-H_2O]^+$ (5), 225 $[M-H_2O-Me]^+$ (25), 187 $[M-C_4H_7O]^+$ (100), 186 $[M-C_4H_8O]^+$ (50), 167 (30). Calc. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02, Found; C, 74.19, H, 6.90%. ^{13}C NMR: see Table 1.

Synthesis of (±)-*faramol.* To a stirred soln of α-naphthol (15 g) in dry dioxane (80 ml) was added gradually BF_3–Et_2O (5 ml) followed by 2-methyl-3-buten-2-ol (8 ml) in dry dioxane (50 ml). The mixture was stirred overnight at room temp. After addition of H_2O (150 ml) the soln was extracted with $CHCl_3$. The $CHCl_3$ soln gave on CC unreacted α-naphtol (6 g) and two other compounds.

1-*Hydroxy-4-prenylnaphthalene* (3 g) mp 66° (from petrol). ^1H NMR (CCl_4): δ1.70 (6H, *s*, 2 Me), 3.52 (2H, *d*, *J* = 6.5 Hz, CH_2), 5.25 (1H, *t*, CH), 6.45 (1H, *d*, *J* = 8.0 Hz, H-2), 6.95 (1H, *d*, *J* = 8.0 Hz, H-3), 7.20–7.50 (2H, *m*, H-6, H-7), 7.70–7.95 (1H, *m*, H-5), 7.95–8.20 (1H, *m*, H-8).

1-*Hydroxy-2-prenylnaphthalene* (**5**, 5 g), oil, ^1H NMR ($CDCl_3$): δ1.77 (6H, *s*, 2Me), 3.47 (2H, *d*, *J* = 7.5 Hz, CH_2), 5.37 (1H, *t*, CH), 7.20–7.50 (4H, *m*, H-3, H-4, H-6, H-7), 7.60–7.90 (1H, *m*, H-5), 7.95–8.25 (1H, *m*, H-8). To a cold soln of **5** (1 g) in $CHCl_3$ (15 ml) was added dropwise an ice-cold soln of *m*-chloroperbenzoic acid (0.75 g) in $CHCl_3$ (15 ml) and the mixture was left at room temp. for 48 hr. The soln was washed with 5% aq. $NaHCO_3$, H_2O and the $CHCl_3$ layer dried. The residue on CC gave unreacted **5**, and two other products: (±)-2,3-*dihydro*-2-(1-*hydroxy*-1-*methylethyl*)-*naphtho*[1,2-*b*]*furan* (**7**, 200 mg), oil. ^1H NMR ($CDCl_3$): δ1.27 (3H, *s*, Me), 1.36 (3H, *s*, Me), 3.13 (2H, *d*, *J* = 9.0 Hz, CH_2), 4.77 (1H, *t*, *J* = 9.0 Hz, CH), 7.20–7.55 (4H, *m*, H-4, H-5, H-7, H-8), 7.60–8.00 (2H, *m*, H-6, H-9), and (±)-3,4-*dihydro*-3-*hydroxy*-2,2-*dimethyl*-2*H*-*naphtho*[1,2-*b*]*pyran* (**8**, 60 mg), identical with the natural product.

Synthesis of (±)-*7-methoxyfaramol.* 1-Hydroxy-5 methoxynaphthalene (1.8 g), obtained by partial methylation of 1,5-dihydroxynaphthalene, was treated as above to give: 1-*hydroxy*-2 *prenyl*-7 *methoxynaphthalene* (**6**, 200 mg), oil. ^1H NMR (CCl_4): δ1.70 (6H, *s*, 2Me), 3.40 (2H, *d*, *J* = 7.5 Hz, CH_2), 3.83 (3H, *s*, OMe), 5.33 (1H, *t*, CH), 6.60 (1H, *d*, *J* = 8.0 Hz, H-6), 7.07 (1H, *d*, *J* = 8.5 Hz, H-3), 7.17 (1H, *t*, *J* = 8.0 Hz, H-7), 7.63 (1H, *d*, *J* = 8.0 Hz, H-8), 7.67 (1H, *d*, *J* = 8.5 Hz, H-4), and 1-*hydroxy*-4-*prenyl*-7-*methoxynaphthalene* (330 mg), oil. ^1H NMR (CCl_4): δ1.70 (1H, *s*, 2Me), 3.77 (3H, *s*, OMe), 3.83 (2H, *d*, *J* = 6.5 Hz, CH_2), 5.30 (1H, *t*, CH), 6.50 (1H, *d*, *J* = 8.0 Hz, H-2), 6.63 (1H, *d*, *J* = 8.0 Hz, H-6), 6.90 (*d*, *J* = 8.0 Hz, H-3), 7.13 (1H, *t*, *J* = 8.0 Hz, H-7), 7.73 (1H, *d*, *J* = 8.0 Hz, H-8). Compound **6** was treated with *m*-CPBA as in the synthesis of (±)-faramol. From the reaction mixture was isolated (±)-3,4-*dihydroxy*-3-*hydroxy*-7-*methoxy*-2,2-*dimethyl*-2*H*-*naphtho*[1,2-*b*]*pyran* (**9**, 20 mg) identical with the natural compound.

Table 1. ^{13}C NMR data for faramol (**8**) and 7-methoxyfaramol (**9**)

C	8	9
2	78.1	78.1
2a	32.3	32.3
2b	26.0	25.9
3	69.8	69.8
4	20.5	20.4
4a	114.5	114.5
5	128.5*	127.5†
6	120.0	113.9
6a	134.2	127.1†
7	128.0*	156.0
8	126.1	104.6
9	125.5	125.6
10	122.2	115.1
10a	126.1	126.1
10b	148.1	148.3
OMe	—	55.6

δ(TMS) = δ$(CD_3)_2CO$ + 29.6 ppm.
*,†Signals may be interchanged.

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ANTHRAQUINONES FROM THE GENUS *CORTINARIUS*

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Key Word Index—*Cortinarius*; *Dermocybe*; basidiomycete; anthraquinones.

Abstract—The anthraquinones 6-methylxanthopurpurin-3-methyl ether, xanthorin, and 1,4-dihydroxy-2-methoxy-7-methyl-9,10-anthraquinone (austrocortinin) have been isolated from fruit bodies of a red Australian toadstool belonging to the genus *Cortinarius*; austrocortinin is reported for the first time as a natural product.

INTRODUCTION

Anthraquinones are found in great variety in toadstools of the genus *Cortinarius* [1] and their occurrence and distribution has proved particularly useful in differentiating infrageneric taxa [2]. While several of the quinones isolated to date such as emodin, physcion, erythroglaucin and endocrocin are also found elsewhere in nature, others such as dermocybin (**1**) [3], dermolutein (**3**) [4], cinnalutein (**4**) [5], dermorubin (**5**) [4] and cinnarubin (**6**) [5] are restricted to *Cortinarius* and in particular to the subgenus *Dermocybe*. The abundance and ease of extraction of these and related* pigments, coupled with their efficient chromatographic separation and rapid identification has led to their use as chemotaxonomic markers during mycological studies of European [7], South American [8] and North American [9] varieties of *Cortinarius* toadstools.

In view of the importance of anthraquinones to the systematics of *Cortinarius* we have examined the anthraquinone content of a red Australian member of this group† and report here the presence of three hydroxylated anthraquinones, **2**, **7** and **8**, which have not previously been reported in *Cortinarius* or in any other genus of *Basidiomycetes*; further, the anthraquinone **8** is a new natural product. We have made a preliminary report elsewhere of the presence in this red toadstool of the novel tetrahydroanthraquinones **9** and **10** [10].

RESULTS AND DISCUSSION

Extraction of fresh, cinnabar-red sporophores of the fungus with alcohol gave a deep red solution which was concentrated, extracted with petrol to remove a lipid fraction consisting largely of triolein (trioleylglycerol) and then with ethyl acetate to remove pigments from the aqueous phase. Preliminary column chromatography separated the less polar anthraquinones from the more

*Many of the fungal anthraquinones are present as, or are accompanied by, their 1-β-D-glucopyranoside derivatives [5, 6].

†Taxonomic difficulties exist within the genus *Cortinarius* and there is a marked confusion in the nomenclature in the subgenus *Dermocybe*. The taxonomy of *Cortinarius* in Australia is severely underdeveloped and the Australian taxa are basically unknown. Voucher specimens of the fungus discussed here are lodged at the herbariums of the NSW Department of Agriculture Biological and Chemical Research Institute, Rydalmere, NSW (accession number DAR 50092) and the Royal Botanic Gardens, Edinburgh, U.K. The fungus has been placed in the subgenus *Dermocybe* close to *Cortinarius* (*Dermocybe*) *sanguineus* (Wulf. ex Fr.) Fr. and *Cortinarius* (*Dermocybe*) *puniceus* Orton [Watling, R., personal communication].