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BACTERIOSTATIC HETEROCYCLES FROM *EUODIA LUNU-ANKENDA**

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Key Word Index—*Euodia lunu-ankenda*; Rutaceae; 8-acetyl-3,4-dihydroxy-5,7-dimethoxy-2,2-dimethylchroman; alloevodionol-7-methyl ether; 4-methoxy-1-methyl-2(1H)quinolinone; isoevodionol; isoevodionol methyl ether; antibacterial activity.

Abstract—A new constituent characterized as 8-acetyl-3,4-dihydroxy-5,7-dimethoxy-2,2-dimethylchroman has been isolated together with alloevodionol-7-methyl ether, 4-methoxy-1-methyl-2(1H) quinolinone, evolitrine, isoevodionol and its methyl ether from the aerial parts of *Euodia lunu-ankenda*. Its structure was confirmed by its transformation to alloevodionol-7-methyl ether. 4-Methoxy-1-methyl-2(1H)quinolinone and its isomer were synthesized by a modified procedure.

INTRODUCTION

The occurrence of diverse classes of compounds in various *Euodia* species and the demonstration of antibacterial activity [1] by a 50% aqueous ethanolic extract of the aerial parts of *Euodia lunu-ankenda*, a hitherto uninvestigated plant, prompted its systematic investigation.

RESULTS AND DISCUSSION

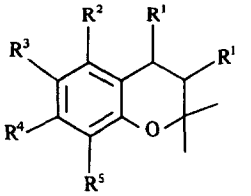
The chloroform-soluble fraction of the ethanolic extract containing the entire biological activity, gave the new chroman **1**, mp 160°, $C_{15}H_{20}O_6$, $[M]^+$ at *m/z* 296, optically inactive. Its ^1H NMR spectrum exhibited the presence of a geminal dimethyl group (δ1.23, 1.43) attached to an oxygen-bearing carbon, an acetyl function (δ2.41; ν_{max}^{KBr} cm^{-1}: 1688) and a lone aromatic proton (δ6.1) presumably flanked by two methoxyl groups (δ3.7, 3.88) and identical in chemical shift to H-6 of alloevodionol-7-methyl ether (**3**) [2]. Besides, two complementary doublets (δ3.70 and 4.72; J = 6 Hz) were assigned to vicinal methines carrying oxygen functions. **1** gave a diacetate **2**, mp 190°, $C_{19}H_{24}O_8$, $[M]^+$ at *m/z* 380. The extent of deshielding experienced by the above methines in **2** (δ5.16 and 5.98) and the magnitude of their coupling constant (J = 4 Hz) revealed the presence of a vicinal diol having a *cis* configuration [3]. On the basis of the foregoing evidence in conjunction with the co-occurrence of **3**, **1** was characterized as 8-acetyl-3,4-dihydroxy-5,7-dimethoxy-2,2-dimethylchroman. On converting **1** into **3** by reacting it with *N,N*-dimethylformamide dimethylacetal [4], its identity was confirmed. Among other isolates characterized from the bioactive fraction were **3**, evolitrine (**4**), a furoquinoline alkaloid, isoevodionol (**5**), isoevodionol methyl ether (**6**) and 4-methoxy-1-methyl-2(1H) quinolinone **7** [5, 6], mp 102°, $C_{11}H_{11}NO_2$, $[M]^+$ at *m/z* 189. For the purpose of a systematic biological study, **7** and its isomer **8** were synthesized by a modified procedure described in the Experimental. Besides the difference in mps, the diagnostic feature in deciding between structures **7** and **8** was the deshielding experienced by H-5 in their ^1H NMR spectra, which in **8**, as in the 4-quinolinones studied so far [7], has acquired a greater deshielding influence of C=O at its *peri* position.

Compounds **1**, **3**, **4**, **7** and **8** exhibited activity [8] against *Bacillus subtilis* and *Staphylococcus aureus*. The minimum inhibitory concentrations (MIC) in μg/ml are: **1** (250), **3** (250), **4** (62.5), **7** (250) and **8** (250).

EXPERIMENTAL

Mps are uncorr. Plant material was collected from Ootacamund, Tamilnadu, India, in October. A voucher specimen has been deposited at the Herbarium in the Botany section of the Institute.

Isolation of constituents. Air-dried powdered plants (aerial



	R^1	R^2	R^3	R^4	R^5	
1	OH	OMe	H	OMe	Ac	
2	OAc	OMe	H	OMe	Ac	
3	H	OMe	H	OMe	Ac	$\Delta^{3,4}$
5	H	OH	Ac	OMe	H	$\Delta^{3,4}$
6	H	OMe	Ac	OMe	H	$\Delta^{3,4}$

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parts) of *E. lunu-ankenda* Merr. (5 kg) were percolated with 95% EtOH which after removal of the solvent *in vacuo* gave a residue (70 g). It was fractionated successively with hexane and $CHCl_3$ to give residues, 30 and 20 g, respectively. CC of the latter over neutral Al_2O_3 (800 g) yielded sitosterol (600 mg); **7** (40 mg); **6** (650 mg), mp 76–77°, $C_{15}H_{18}O_4$, $[M]^+$ *m/z* 262 [9]; **3** (30 mg), mp 105°, $C_{15}H_{18}O_4$, $[M]^+$ *m/z* 262; **5** (1.1 g), mp 128–29°, $C_{14}H_{16}O_4$, $[M]^+$ *m/z* 248 [9]; **1** (110 mg); **4** (50 mg), mp 114°, $C_{13}H_{11}NO_3$, $[M]^+$ *m/z* 229 [10].

8-*Acetyl*-3,4-*dihydroxy*-5,7-*dimethoxy*-2,2-*dimethylchroman* (**1**). Eluted with EtOAc, mp 160° (Me_2CO): UV λ_{max}^{MeOH} nm (log ε): 229 (4.1), 275 (4.0); IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 1688 (C=O), 1603, 1575, 1472, 1452, 1278, 1095, 810, 715; MS *m/z* (rel. int.): 296 $[M]^+$, 281, 278, 263, 250, 247, 235, 225 (100), 209, 207, 193, 179, 149.

3,4-*Diacetoxy*-8-*acetyl*-5,7-*dimethoxy*-2,2-*dimethylchroman* (**2**) was obtained by reacting **1** with Ac_2O/pyridine, mp 190° (C_6H_6–hexane); $C_{19}H_{24}O_8$, $[M]^+$ *m/z* 380; ^1H NMR (90 MHz, $CDCl_3$): δ 1.30 and 1.43 (*s*, geminal Me_2), 2.05, 2.08 (*s*, OAc), 2.46 (*s*, OAc), 3.83 (*s*, 2 OMe), 5.16 and 5.98 (*d*, 1H each, H-3 and H-4, respectively; J = 4 Hz), 6.1 (*s*, H-6).

Conversion of **1** *into* **3**. A mixture of **1** (100 mg; 0.34 mM) and *N*,*N*-dimethylformamide dimethylacetal (3.4 mM) in CH_2Cl_2 (20 ml) was stirred for 2 hr. The solvents were removed, the residue was taken in toluene, treated with MeI (2 ml) and the suspension refluxed for 1 hr. After removal of solvent, the residue was chromatographed over a column of neutral Al_2O_3 to afford **3** (C_6H_6–EtOAc, 9:1) (25 mg).

Synthesis of **7** *and* **8**. *N*-Methyl cyanoacetanilide (2 g) was heated with conc. HCl (10 ml) at 55° for 4 hr. The cold reaction mixture was filtered, HCl removed *in vacuo* and the residue (1.8 g) crystallized to afford *N*-methyl malonanilide, mp 120° (CH_2Cl_2–hexane) [11]. The latter (500 mg) was mixed with PPA (8 g) and heated at 100° for 4 hr. The cold reaction mixture was diluted with H_2O, the solid filtered and crystallized from EtOH to give 4-hydroxy-1-methyl-2(1H) quinolinone (270 mg), mp 270° [12]. This, on treatment with CH_2N_2, gave **7** and **8** [13]. **8**, mp 195°; $C_{11}H_{11}NO_2$, $[M]^+$ *m/z* 189; ^1H NMR ($CDCl_3$): δ 3.58 (*s*, N-Me), 3.88 (*s*, OMe), 6.75 (*s*, H-3), 7.42 (*m*, H-6, H-7, H-8), 8.35 (*dd*, H-5, J = 2 and 8 Hz).

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