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TWO CHROMENES FROM *EVODIA LEPTA*

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Key Word Index—*Evodia lepta*; Rutaceae; chromenes; leptonol; methylleptol A; alloevodione.

Abstract—Two new chromenes named, leptonol and methylleptol A, along with four known compounds, alloevodione, 7, 4-dihydroxy-3, 5, 3′-trimethoxyflavone, 3, 7-dimethylkaempferol and clovandiol, have been isolated from *Evodia lepta*. Their structures were elucidated by spectroscopic analysis and chemical techniques.

INTRODUCTION

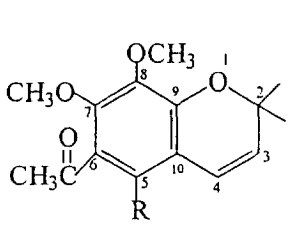
Our previous study has resulted in the isolation and structural elucidation of three new compounds (leptol A, ethylleptol A and leptene A) and two known compounds (isoevodionol and evodione) [1] from the traditional Chinese herb, *Evodia lepta*. As a part of our continuing research into the same material, we now wish to report the isolation and structural elucidation of two new chromenes, leptonol (**1**) and methylleptol A (**2**), and one known chromene, alloevodione (**3**).

RESULTS AND DISCUSSION

Leptonol (**1**) was obtained as an orange oil. Its ^{1}H NMR spectrum was very similar to that of evodione, except that the hydroxyl signal (δ 13.57) in compound **1** was substituted by that of methoxyl group. Because methylation of **1** using $(CH_3)_2SO_4$–K_2CO_3-acetone [2] gave evodione (**1a**), the acetyl group in **1** was assigned to position 6. A chelated phenolic hydroxyl signal at δ 13.57 in its ^{1}H NMR spectrum and a chelated carbonyl group absorption at 1640 cm^{-1} in its IR spectrum, demonstrated that the hydroxyl group was at position 5 or 7. Acetylation of **1** using acetic anhydride-pyridine afforded **1b**. The upfield shift of H-4 ($\Delta\delta$=0.42) in the ^{1}H NMR spectrum after acetylation of **1** indicated that the hydroxyl group was at position 5, according to the rules of Arnone [3]. Thus, leptonol (**1**) was determined as 5-hydroxyl-6-acetyl-7,8-dimethoxy-2,2-dimethyl-2H-[1]-benzopyran.

Methylleptol A (**2**) was colourless oil. Its ^{1}H NMR spectrum showed the presence of a methoxyl group at δ 3.18 (3H, *s*); other signals were similar to those of leptol A, a chromene from the same material [1]. The EI mass spectrum of this compound indicated the $[m]^+$ at *m/z* 308, which was 14 mu more than that of leptol A. The IR spectrum demonstrated that this compound had no hydroxyl group. From the above results, we could infer methylleptol A was the product of methylation of leptol A. Methylation of leptol A using methanol-formic acid method gave methylleptol A, and this confirmed the above inference. Thus, the structure of methylleptol A (**2**) was elucidated as 6-(1′-methoxyethyl)-5,7,8-trimethoxy-2,2-dimethyl-2H-[1]-benzopyran.

Alloevodione (**3**) was isolated as pale yellow oil. Its ^{1}H NMR spectrum was almost identical to that of evodione (**1a**) [1], except for small chemical shift difference. They also had the same $[m]^+$ and main fragment ions peaks in their EI mass spectra [1]. These data suggested that they had the same skeleton and substituted groups, but they were not the same because they had different TLC^{Rf} values. (silica gel, petrol-EtOAc, 12:1). The difference in their structure was the position of the acetyl group. We cannot identify compound **3** as alloevodione, which is a known natural product from *E. elleyana* [4], without further study, because the ^{1}H NMR spectrum of compound **3** was different from that of alloevodione given in the literature [5]. Reduction of **3** using $NaBH_4$-MeOH method gave compound **3a**. In the HMBC spectrum of compound **3a**, H-4 was correlated with the carbons at δ 149.5 and 147.4, respectively, and the proton of one methoxyl group at δ 3.82 was also correlated with the carbon at δ 149.5. This suggested that the carbon at δ 149.5 should be assigned to C-5 and the carbon at δ 147.4 should be assigned to C-9. Because H-1′ was correlated with the carbons at δ 147.4 (C-9), δ 152.5 and δ 123.4, C-1′ should be attached to C-8. The carbon at δ 152.5 should be assigned to C-7, and the carbon at δ 123.4 to C-8. Because compound **3a** was the product of reduction of compound **3**, the acetyl group in compound **3a** should be placed at

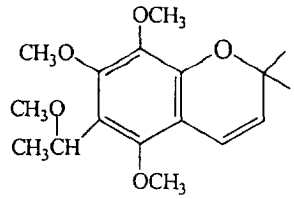


R

1 —OH

1a —OCH_3

1b —$OCOCH_3$



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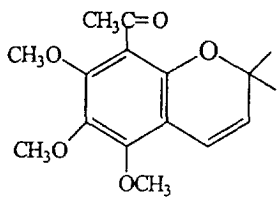

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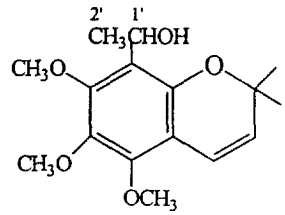
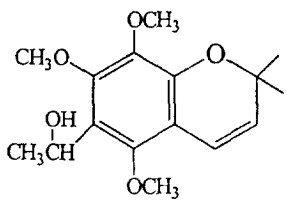
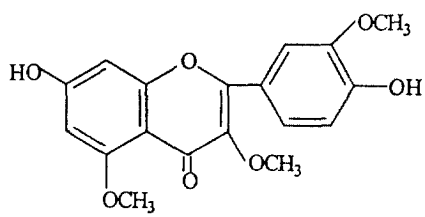


3a



leptol A



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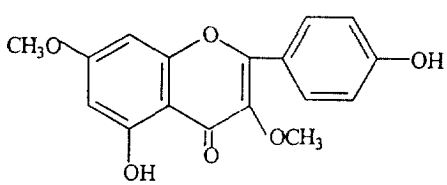

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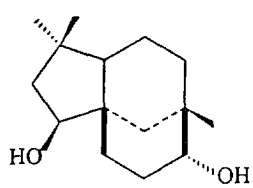

6

position 8. From above results, compound **3** was identified as 5, 6, 7-trimethoxy-8-acetyl-2, 2-dimethyl-2H[1]-benzopyran, a known compound from *E. ellerya*.

Compounds **4**, **5**, and **6** were identified as 7, 4′-dihydroxy-3, 5, 3′-trimethoxyflavone [6], 3, 7-dimethylkaempferol [7] and clovandiol [8], respectively, by comparison of their spectral data with those of the corresponding compounds reported in the literature.

EXPERIMENTAL

General

EIMS: 70 eV, direct inlet. ^{1}H NMR: 400 MHz, $CDCl_3$ and CD_3COCD_3. ^{13}C NMR: 100 MHz, $CDCl_3$ and CD_3COCD_3. Chemical shifts are given in δ and were referred in $CDCl_3$ to the residual $CHCl_3$ (δ 7.24 for ^{1}H, 77.0 for ^{13}C) and in CD_3COCD_3 to the residual Me_2CO (δ 2.05 for ^{1}H, 29.8 for ^{13}C).

Plant material

Aerial parts of *E. lepta* (Spreng) Merr. were collected from Hainan province, P. R. China, in July, 1992. A voucher sample (910042) is deposited in the Herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences. A specimen was authenticated by Dr Xiao-qiang Ma, Department of Phytochemistry, Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

Extraction and isolation

Dried and powdered aerial parts (10 kg) were extracted ×2 with 95% EtOH at room temp. over 2 weeks. The combined extracts were evapd to dryness under red. pres. (35°) and the residue obtained (250 g) was subjected to CC over silica gel, eluting with petrol-EtOAc (10:1) to give an orange oil (80 g), and then eluting with $CHCl_3$ to give a dark gum (65 g). Part of this oil (20 g) was fractionated by silica gel CC eluting with a petrol-EtOAc gradient. The frs obtained were repeatedly chromatographed by silica gel CC using a petrol-EtOAc mix. and finally purified by silica gel CC using petrol-EtOAc (12:1) to give **1** (534 mg), petrol-EtOAc (15:1) to give **3** (108 mg) and petrol-Me_2CO (20:1) to give **2** (50 mg). The $CHCl_3$ part (65 g) was fractionated by silica gel CC eluting with a CH_2Cl_2-EtOAc gradient. Compounds **4** (10 mg) and **5** (15 mg) were isolated from frs. 4 by silica gel CC eluting with CH_2Cl_2-EtOAc (6:1). Compound **4** was purified by Sephadex LH-20 CC using $CHCl_3$–MeOH (10:1) as eluant. Fr. 5 was subjected to repeated CC over silica gel eluting with CH_2Cl_2–Me_2CO (5:1) to give compound **6** (5 mg).

Leptonol (**1**)

$C_{15}H_{18}O_5$. Yellow oil. $\lambda MeOH_{max}$ nm (logϵ): 208 (4.17), 263 (4.47), 311 (4.01), 354 (3.58). IR $\nu film_{max}$ cm^{-1}: 2970, 2930, 1640, 1600, 1378, 1364, 1200, 1055. ^1H NMR ($CDCl_3$): δ 13.57 (1H, *s*, OH-5), 6.65 (1H, *d*, J=10.1 Hz, H-4), 5.49 (1H, *d*, J=10.1 Hz, H-3), 3.97 (3H, *s*, $-OCH_3$), 3.76 (3H, *s*, $-OCH_3$), 2.61 (3H, *s*, $-COCH_3$), 1.47 (6H, *s*, *gem*-dimethyl). ^{13}C NMR ($CDCl_3$): δ 203.5 (C=O), 156.4, 155.6, 153.8, 134.1, 126.6 (C-3), 116.0 (C-4), 108.2, 105.9, 78.3 (C-2), 61.1 (-OCH_3), 61.1 ($-OCH_3$), 32.0 ($-COCH_3$), 28.3 (CH_3-2). EIMS *m/z* (rel. int.): 278 $[M]^+$ (21), 263 (100), 233 (7).

Acetyleptonol (**1b**)

$C_{17}H_{20}O_6$. Pale yellow oil. ^1H NMR ($CDCl_3$): δ 6.23 (1H, *d*, J=9.9 Hz, H-4), 5.60 (1H, *d*, J=9.9 Hz, H-3), 3.92 (3H, *s*, $-OCH_3$), 3.84 (3H, *s*, $-OCH_3$), 2.46 (3H, *s*, $-COCH_3$), 2.24 (3H, *s*, $-OCOCH_3$), 1.46 (6H, *s*, *gem*-dimethyl). EIMS *m/z* (rel. int.): 320 $[M]^-$ (17), 278 (53), 263 (100), 235 (25).

Methylleptol A (**2**)

$C_{17}H_{24}O_5$. Colourless oil. $[\alpha]^{26}_D$ = +0.089° (CH_3COCH_3; *c* 0.450). IR $\nu film_{max}$ cm^{-1}: 2980, 2930, 1740, 1635, 1593, 1471, 1375, 1360, 1194, 1136, 1053, 978. ^1H NMR (CD_3COCD_3): δ 6.54 (1H, *d*, J=9.8 Hz, H-4), 5.73 (1H, *d*, J=9.8 Hz, H-3), 4.71 (1H, *q*, J=6.7 Hz, H-1′), 3.81 (6H, *s*, 2× $-OCH_3$), 3.69 (3H, *s*, $-OCH_3$), 3.18 (3H, *s*, H-1″), 1.52 (3H, *d*, J=6.7 Hz, H-2′), 1.47 (3H, *s*, CH_3-2), 1.44 (3H, *s*, CH_3-2). EIMS *m/z* (rel. int.): 308 $[M]^+$ (16), 293 $[M-CH_3]^+$ (100), 276 (15), 263 (30), 261 (71), 245 (15), 231 (30).

Alloevodione (**3**)

$C_{16}H_{20}O_5$. Pale yellow oil. $\lambda MeOH_{max}$ nm (logϵ): 220 (4.34), 254 (4.13), 321 (3.52). IR $\nu film_{max}$ cm^{-1}: 2970, 2940, 1702, 590, 1458, 1387, 1362, 1292, 1050. ^1H NMR ($CDCl_3$): δ 6.51 (1H, *d*, J=10.0 Hz, H-4), 5.54 (1H, *d*, J=10.0 Hz, H-3), 3.87 (3H, *s*, $-OCH_3$), 3.85 (3H, *s*, $-OCH_3$), 3.80 (3H, *s*, $-OCH_3$), 2.47 (3H, *s*, CH_3CO-7), 1.39 (6H, *s*, *gem*-dimethyl). ^{13}C NMR ($CDCl_3$): δ 200.7 (C=O), 150.6, 150.3, 145.8 (C-9), 139.8, 129.2 (C-3), 121.1 (C-7), 116.4 (C-4), 111.3 (C-10), 76.6 (C-2), 62.1 (-OCH_3), 61.4 ($-OCH_3$), 61.1 ($-OCH_3$), 32.5 ($-COCH_3$), 27.8 (CH_3-2). EIMS *m/z* (rel. int.): 292 $[M]^+$ (31), 277 $[M-CH_3]^+$ (100), 247 (29).

Compound **3a**

$C_{16}H_{22}O_5$. Pale yellow oil. IR $\nu film_{max}$ cm^{-1}: 3558, 2974, 2930, 1639, 1595, 1466, 1417, 1344, 1281, 1132, 1034, 997. ^1H NMR (CD_3COCD_3): δ 6.53 (1H, *d*, J=10.0 Hz, H-4), 5.67 (1H, *d*, J=10.0 Hz, H-3), 5.06 (1H, *q*, J=6.7 Hz, H-1′), 3.86 (3H, *s*, $-OCH_3$), 3.82 (3H, *s*, $-OCH_3$), 3.77 (3H, *s*, $-OCH_3$), 1.45 (3H, *d*, J=6.7 Hz, H-2′), 1.41 (6H, *s*, *gem*-dimethyl). ^{13}C NMR (CD_3COCD_3): δ 152.5 (C-7), 149.5 (C-5), 147.4 (C-9), 141.2 (C-6), 130.3 (C-3), 123.4 (C-8), 117.8 (C-4), 112.5 (C-10), 77.4 (C-2), 64.4 (C-1′), 62.1 ($-OCH_3$), 62.0 ($-OCH_3$), 61.4 ($-OCH_3$), 28.2 (CH_3-2), 27.94 (CH_3-2), 25.0 (C-2′). EIMS *m/z* (re. int.): 294 $[M]^+$ (17), 279 $[M-CH_3]^+$ (100), 261 (12), 231 (8).

Methylation of **1** to give evodione

Compound **1** (20 mg) in dry Me_2CO (1 ml) was refluxed with Me_2SO_4 (50 μl) in the presence of dry K_2CO_3 (120 mg) for 4 hr, then filtered, inorganic salts washed out with hot Me_2CO and combined, filtered and conc. The residue was subjected to CC eluting with petrol-EtOAc (10:1) to give evodione (**3**) (15 mg), yield 70%. IR, MS and ^1H NMR data identical to natural product.

Synthesis of **2** from leptol A

Leptol A (30 mg) was dissolved in MeOH (3 ml) and HCO_2H (0.5 ml) added to the soln. The mixt. was

stirred continuously for 5 hr at room temp., neutralized with satd $NaHCO_3$ soln, extracted with Et_2O, the organic layer washed with brine and dried (Na_2SO_4). Removal of solvent gave a residue which was subjected to CC using petrol-EtOAc (8:1) to furnish **2** (28 mg), yield 89%.

Reduction of alloevodione (**3**) *to give compound* **3a**

Alloevodione (30 mg) was dissolved in 4 ml of MeOH and $NaBH_4$ (340 mg) added to this soln in ten batches at room temp. The mixt. was stirred continuously for 5 hr at room temp. after addition of $NaBH_4$ was complete. MeOH was then removed and the residue dissolved in EtoAc (15 ml) and H_2O. The EtoAc layer was separated and concd; the residue after silica gel CC eluting with petrol-EtOAc (10:1) gave compound **3a** (23 mg), yield 76%.

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