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10-*O*-BENZOYLTHEVESIDE AND 10-DEHYDROGENIPOSIDE FROM THE LEAVES OF *CERBERA MANGHAS**

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Key Word Index—*Cerbera manghas*; Apocynaceae; iridoid; theviridoside; theveside; benzoyltheveside; dehydrogeniposide; loganin.

Abstract—10-*O*-Benzoyltheveside and 10-dehydrogeniposide were isolated from the fresh leaves of *Cerbera manghas* along with loganin, theviridoside and theveside. The structures were established by spectral and chemical methods.

INTRODUCTION

In the course of our studies on the constituents of *Cerbera*, we have isolated cardiac glycosides [1–4] lignans [5–7] normonoterpenoids [8], and yellow pigments with an iridoid skeleton [9]. This paper deals with the isolation of two minor iridoids, 10-*O*-benzoyltheveside (**1**) and 10-dehydrogeniposide (**2**), along with loganin (**3**) and the major iridoids theviridoside (**4**) and theveside (**5**) [10] from fresh leaves of *C. manghas*.

RESULTS AND DISCUSSION

Compound **1** was obtained from the MeOH homogenate of the leaves by column chromatography (reversed and normal phases). On TLC, it showed a polarity intermediate between **4** and **5** and gave the same staining reaction as these two compounds. Upon methylation with diazomethane, **1** afforded a methyl ester (**1a**) which gave an $[M+Na]^+$ peak at *m/z* 531.147 ($C_{24}H_{28}O_{12}$ + Na), and ^{1}H NMR signals due to **4** and a benzoyl group. A downfield shift of the signals due to H-10a,b (+0.68 and +0.58 ppm, respectively), suggested the molecular formula of a benzoate of **4**. In order to confirm the structure of **1** to be that of benzoyltheveside, **1** was deacylated (NaOMe–MeOH), followed by methylation (CH_2N_2). The product was identified as **4** by TLC and HPLC. Methylation of **1**-acetate (**1b**) afforded a **1a**-pentacetate ($[M+Na]^+$ peak at *m/z* 741). Comparison of the ^{13}C NMR spectrum of **1a** with that of **4** showed that C-10 and C-8 were shifted downfield (+2.5 ppm) and upfield (−6.6 ppm), respectively. The structure of **1** was thus determined to be 10-*O*-benzoyltheveside.

Compound **2** showed the same polarity and staining reaction as **3** on TLC. In the ^{1}H NMR spectrum of **2**, one formyl proton signal was observed at δ9.83 (*s*) together with two trisubstituted olefinic proton signals at δ7.69 (*s*) and 6.82 (*dd*, *J* = 5, 2 Hz), which were assignable respectively to H-3 and H-7 of an iridoid skeleton. The presence of one each of a formyl and a carbomethoxyl function and a glucosyl group was confirmed by the ^{1}H and ^{13}C NMR spectra. As the FAB mass spectrum afforded an $[M+Na]^+$ peak at *m/z* 409.112 ($C_{17}H_{22}O_{10}$ + Na), 2H less than geniposide, **2** was proposed to be dehydrogeniposide, and this was finally confirmed by $NaBH_4$ reduction of **2** to afford geniposide.

Due to deacylation during the air-drying process, **1** is barely detectable in air-dried leaves, and no **4**-benzoate was observed in the methanol homogenates from either fresh leaves or air-dried leaves.

EXPERIMENTAL

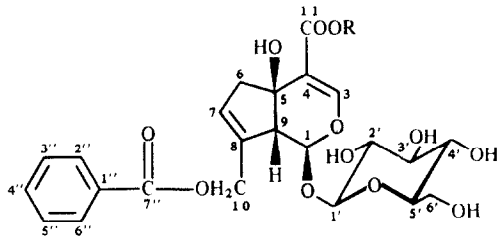
General. NMR: 400 and 100 MHz, pyridine-d_5, TMS int std; TLC and silica gel CC: 1: $CHCl_3$–MeOH–H_2O (7:3:1, bottom layer), 2: EtOAc–MeOH–H_2O (8:2:1); HPLC: radial pack C_{18} column, MeCN–H_2O (5–20%) at 1.0 ml min^{-1}.

Extraction and isolation of iridoids. Fresh leaves of *C. manghas* L. harvested in Singapore in January 1986, (2.6 kg), were homogenized with MeOH and further percolated with MeOH. The MeOH percolate was concd *in vacuo* and extracted with BuOH. The BuOH extractives were partitioned with C_6H_6 and the C_6H_6-insolule fraction (22.8 g) was then chromatographed on a polystyrene column (MCI-gel, CHP-20) with MeOH/H_2O as solvent. The 100% H_2O (2.6 g) eluate was chromatographed on an ODS column with MeCN–H_2O to give **1** (23 mg) and **5** (270 mg). The 20% MeOH eluate yielded, **2** (20 mg), **3** (20 mg) and **4** (60 mg) by CC on ODS with MeCN–H_2O.

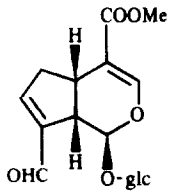
10-O-*Benzoyltheveside* (**1**). Solid, ^{1}H NMR δ: 5.96 (1H, *br*, *s*, H-7), 7.40 (2H, *t*, *J* = 8 Hz, H-3″,5″), 7.48 (1H, *t*, *J* = 8 Hz, H-4″), 7.89 (1H, *s*, H-3), 8.15 (2H, *d*, *J* = 8 Hz, H-2″,6″).

To a soln of **1** (10 mg) in MeOH (1 ml), CH_2N_2 in Et_2O was added. After standing for 1 hr at room temp., the solvent was evapd *in vacuo* and the residue purified by silica gel CC (solvent 1, 7:2:2) to give **1**-methylate (**1a**) as a homogeneous solid, $[\alpha]_D^{26}$ −28.5° (MeOH; *c* 0.85). FABMS *m/z*: 531.147 $C_{24}H_{28}O_{12}$ + Na requires 531.148. ^{1}H NMR δ: 2.91, 3.28 (1H each, *br d*, *J* = 17 Hz, H-6a,b), 3.44 (1H, *d*, *J* = 9 Hz, H-9), 3.63 (3H, *s*, –COOMe), 4.00 (1H, *m*, H-5′), 4.11, 4.22, 4.27 (1H ea, *t*, *J* = 9 Hz, H-2′, 3′, 4′), 4.32 (1H, *dd*, *J* = 5, 12 Hz, H-6′a), 4.50 (1H, *dd*, *J* = 12, 2 Hz, H-6′b), 5.19, 5.37 (1H, ea, *br*, *d*, *J* = 15 Hz, H-10a, b), 5.40 (1H, *d*, *J* = 8 Hz,

*Part 10 in the series, '*Cerbera*'. For Part 9, see ref. [8].



1 R = H
1a R = Me
1b : **1** - pentaacetate
1c : **1a** - pentaacetate



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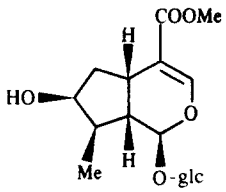

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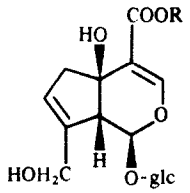

4 R = Me
5 R = H

H-1'), 5.69 (1H, *d*, $J = 8$ Hz, H-1), 5.91 (1H, *br s*, H-7), 7.38 (2H, *t*, $J = 8$ Hz, H-3'',5''), 7.49 (1H, *t*, $J = 8$ Hz, H-4''), 7.66 (1H, *s*, H-3), 8.14 (2H, *d*, $J = 8$ Hz, H-2'',6''); ^{13}C NMR δ: 47.9 (C-6), 50.7 (-COOCH$_3$), 57.6 (C-9), 62.7 (C-6'), 63.4 (C-10), 71.5 (C-4'), 74.8 (C-2'), 76.2 (C-5), 78.3, 78.9 (C-3',5'), 99.4 (C-1), 101.0 (C-1'), 115.3 (C-4), 128.7, 129.9 (C-2'',3'',5'',6''), 128.8 (C-7), 130.7 (C-1''), 133.2 (C-4''), 136.7 (C-8), 152.3 (C-3), 166.1, 166.9 (C-11, C-7'').

To a soln of **1** (50 mg) in MeOH (2 ml), 2.5% NaOMe in MeOH (0.5 ml) was added. The mixture was allowed to stand at room temp. for 3 hr, diluted with MeOH, and neutralized with IR-120B. The soln was concd *in vacuo* and the residue methylated with CH_2N_2 in the same manner as described above. The methyl ester was purified on a silica gel column (solvent 1, 35:10:7) and identified as **4** by TLC (solvents 1, 7:3:1; 2, 8:2:1) and HPLC (C_{18} column, 14% MeCN).

Compound **1** (50 mg) was acetylated with 0.5 ml each of pyridine and Ac_2O at room temp. for 20 hr. The acetate was then methylated with CH_2N_2 in the same manner as described above, and the product was finally purified on a silica gel column (solvent C_6H_6–Me_2CO) to afford a homogeneous solid. $[\alpha]_D^{27}$ −26.7° (MeOH; *c* 1.18), FABMS *m/z*: 741 ($C_{34}H_{38}O_{17}$ + Na).

10-Dehydrogeniposide (**2**). Solid, $[\alpha]_D^{25}$ + 43.3° (MeOH; *c* 1.10), FABMS *m/z*: 409.112 $C_{17}H_{22}O_{10}$ + Na requires 409.111. ^{1}H NMR δ: 2.56 (1H, *br d*, $J = 18$ Hz, H-6a), 2.84 (1H, *ddt*, $J = 18$, 8, 2 Hz, H-6b), 3.44 (1H, *br*, *d*, $J = 18$ Hz, H-6a), 2.84 (1H, *ddt*, $J = 18$, 8, 2 Hz, H-6b), 3.44 (1H, *ddd*, $J = 8$, 8, 3 Hz, H-5), 3.50 (1H, *br d*, $J = 8$ Hz, H-9), 3.57 (3H, *s*, -COOMe), 3.90 (1H, *m*, H-5'), 4.02 (1H, *dd*, $J = 9$, 8 Hz, H-2'), 4.21 (1H, *t*, $J = 9$ Hz, H-3'), 4.27 (1H, *t*, $J = 9$ Hz, H-4'), 4.35 (1H, *dd*, $J = 12$, 5 Hz, H-6'a), 4.45 (1H, *dd*, $J = 12$, 2 Hz, H-6'b), 5.28 (1H, *d*, $J = 8$ Hz, H-1'), 6.47 (1H, *d*, $J = 4$ Hz, H-1), 6.82 (1H, *dd*, $J = 5$, 2 Hz, H-7), 7.69 (1H, *s*, H-3), 9.83 (1H, *s*, H-10); ^{13}C NMR δ: 33.6 (C-5), 39.6 (C-6), 46.1 (C-9), 50.9 (-COOMe), 62.5 (C-6'), 71.3 (C-4'), 74.6 (C-2'), 78.6, 78.4 (C-3',5'), 94.6 (C-1), 101.2 (C-1'), 111.2 (C-4), 144.5 (C-8), 152.7 (C-3), 154.8 (C-7), 167.1 (C-11), 189.4 (C-10).

To **2** (8 mg) in MeOH (1 ml), $NaBH_4$ (20 mg) was added and the mixture stirred for 30 min at 0°. The mixture was diluted with H_2O and then extracted with BuOH. The BuOH layer was concd *in vacuo*. The residue showed the same R_f value as geniposide on TLC (solvent 1, 7:3:1).

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