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CAFFEOYL DERIVATIVES OF A SUGAR LACTONE AND ITS HYDROXY ACID FROM THE LEAVES OF *BIDENS PILOSA*

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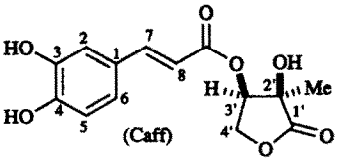
Key Word Index—*Bidens pilosa*; Compositae; sugar lactone; hydroxy acid; 2-*C*-methyl-D-erythrono-1,4-lactone; 2-*C*-methyl-D-erythronic acid; caffeic acid conjugates.

Abstract—A new sugar lactone derivative, 3-*O*-caffeoyl-2-*C*-methyl-D-erythrono-1,4-lactone, and three new hydroxy acid derivatives, 2-*O*-caffeoyl-2-*C*-methyl-D-erythronic acid, methyl 2-*O*-caffeoyl-2-*C*-methyl-D-erythronic acid, and methyl 3-*O*-caffeoyl-2-*C*-methyl-D-erythronic acid were isolated from the leaves of *Bidens pilosa*. Their structures were elucidated on the basis of chemical and spectral evidence, Two methyl esters are thought to be artefacts.

INTRODUCTION

Previously, we reported the aurone glucosides and the phenylpropanoid glucosides from the leaves of *Bidens pilosa* [1]. Further study on the chemical constituents of the plant have led to the isolation of four new compounds, a caffeoyl ester of a sugar lactone and three caffeoyl esters of a hydroxy acid corresponding to the sugar lactone.



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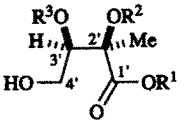

	R^1	R^2	R^3
2	H	Caff	H
3	Me	Caff	H
4	Me	H	Caff

RESULTS AND DISCUSSION

Compound **1** was obtained as a pale yellow solid. Its high-resolution EI mass spectrum (HR-EIMS) gave the molecular formula $C_{14}H_{14}O_7$. The ^{1}H NMR signals (see Experimental) and the EI mass spectral fragments (*m/z* 180 and 163) indicated that **1** has a caffeoyl group. The ^{1}H NMR signals appearing as an ABX (δ4.61, *dd*, $J=11.2$ and 4.2 Hz; δ4.33, *dd*, $J=11.2$ and 1.2 Hz; δ5.30, *dd*, $J=4.2$ and 1.2 Hz), a methyl singlet (δ1.51) and the IR absorption at 1780 cm^{-1} suggested that the residual structure was a 2,3-dihydroxy-2-methyl-γ-lactone. The relative configuration was determined to be erythro because of the presence of the NOE between H-3′ and H_3-5′. The sugar lactone obtained by acid hydrolysis of **1** with 2 N HCl showed the spectral data ($[\alpha]_D$, IR and ^{1}H NMR) identical with those of 2-*C*-methyl-D-erythrono-1,4-lactone [2–4]. Because the ^{1}H NMR spectral data of H-3′ of **1** appeared at δ5.30, the caffeoyl group must be attached to the 3′-hydroxyl function of the sugar lactone. Thus, the structure of **1** was elucidated to be 3-*O*-caffeoyl-2-*C*-methyl-D-erythrono-1,4-lactone.

Compound **2** was obtained as a solid. The HR-EI mass spectrum of **2** showed its formula to be $C_{14}H_{16}O_8$. The EI mass spectrum indicated the presence of a caffeoyl group in **2**. The ^{13}C NMR spectral data of **2**, which were closely related to **1** except for the signal due to C-4′, and the increment of H_2O in the formula suggested that **2** is the caffeoyl derivative of the hydroxy acid corresponding to 2-*C*-methyl-D-erythrono-1,4-lactone. It was deduced that the caffeoyl group was attached to the 2′-hydroxyl because the ^{1}H NMR signals due to the H-3′ and H_2-4′ appeared at δ4.04 and 4.26. Treatment of **2** with 1 M CF_3COOH caused the lactone formation involving the acyl migration to afford **1**. Thus, **2** was determined to be 2-*O*-caffeoyl-2-*C*-methyl-D-erythronic acid.

Compounds **3** and **4** were obtained as a pale yellow viscous liquid. Their ^{1}H and ^{13}C NMR spectra, which resembled those of **2**, suggested that each compound consists of a caffeoyl group and a methyl 2-*C*-methylerythronate. Assignment of the chemical shifts of the hydroxy acid in **3** and **4** indicated that the caffeoyl moiety is attached to the 2′- and the 3′-hydroxyl functions, respectively. Treatment of **1** with MeOH under reflux gave **3** and **4**. Thus, the structures of **3** and **4** were decided to be methyl 2-*O*-caffeoyl-2-*C*-methyl-D-erythronate and methyl 3-*O*-caffeoyl-2-*C*-methyl-D-erythronate, respectively.

Sugar lactones have been isolated previously from the aerial part of *Astragarus lusitanicus* [4], the leaves of water-stressed *Cicer arietinum* [5] and the aerial part of *Oryza sativa* [2], and sugar-related hydroxy acids have been isolated from the leaves of *Phaseolus vulgaris* and *Trifolium incarnatum* [6]. This appears to be the first report of the isolation of caffeoyl derivatives of sugar lactones and related hydroxy acids. Since refluxing of **1** in methanol gave **3** and **4**, it seems that both of them were formed from **1** during the isolation procedure. The 3-*O*-caffeoyl derivative of the free acid corresponding to **4** has not been isolated and **1** did not form during the isolation of **2**. Therefore both **1** and **2** were considered to be natural components in the plant.

EXPERIMENTAL

The concd MeOH extract of the fresh leaves of *Bidens pilosa* (2.0 kg, collected in Hinoshi, Tokyo in November 1986) was partitioned between BuOH and H_2O. A part (*ca* 1 g) of the concd BuOH phase was chromatographed over ODS column. Elution with MeOH–H_2O and MeCN–H_2O systems yielded **1** (23 mg), **2** (14 mg), **3** (6.1 mg) and **4** (13 mg).

3-O-*Caffeoyl*-2-C-*methyl*-D-*erythrono*-1,4-*lactone* (**1**). $[\alpha]_D^{25}$ −93.3° (MeOH; *c* 0.80). λ_{max}^{MeOH} nm (log ε): 206sh (3.98), 220 (4.08), 234sh (3.92), 246 (3.95), 304sh (4.08), 332 (4.21). EIMS *m/z* (rel. int.): 294 (28), 180 (22), 163 (100), 162 (36), 149 (8), 135 (22), 134 (50), 117 (12), 89 (32). HR-EIMS: *m/z* 294.0709 $[M]^+$, calc. for $C_{14}H_{14}O_7$: 294.0739. IR ν_{max}^{KBr} cm^{-1}: 3400, 1780, 1704, 1633, 1604, 1526, 1445, 1372, 1269, 1218, 1162, 1118, 982. ^1H NMR (400 MHz, CD_3OD): δ 7.63 (1H, *d*, *J* = 15.9 Hz, H-7), 7.06 (1H, *d*, *J* = 2.0 Hz, H-2), 6.96 (1H, *dd*, *J* = 8.2, 2.0 Hz, H-6), 6.78 (1H, *d*, *J* = 8.2 Hz, H-5), 6.32 (1H, *d*, *J* = 15.9 Hz, H-8), 5.30 (1H, *dd*, *J* = 4.2, 1.2 Hz, H-3′), 4.61 (1H, *dd*, *J* = 11.2, 4.2 Hz, H_A-4′), 4.33 (1H, *dd*, *J* = 11.2, 1.2 Hz, H_B-4′), 1.51 (3H, *s*, H_3-5′). ^{13}C NMR (100 MHz, CD_3OD): δ 127.8 (C-1), 115.4 (C-2), 146.9 (C-3), 149.8 (C-4), 116.6 (C-5), 123.2 (C-6), 148.1 (C-7), 114.4 (C-8), 168.0 (C=O), 179.2 (C-1′), 73.6 (C-2′), 76.1 (C-3′), 71.1 (C-4′), 22.4 (C-5′).

2-O-*Caffeoyl*-2-C-*methyl*-D-*erythronic acid* (**2**). $[\alpha]_D^{24}$ −7.3° (MeOH; *c* 0.73). EIMS *m/z* (rel. int.): 312, 294 (28), 180 (40), 163 (100), 134 (42), HR-EIMS: *m/z* 312.0783 $[M]^+$, calc. for $C_{14}H_{16}O_8$: 312.0845; 294.0683 $[M-H_2O]^+$, calc. for $C_{14}H_{14}O_7$: 294.0739. IR ν_{max}^{KBr} cm^{-1}: 3407, 1701, 1607, 1524, 1449, 1367, 1284. ^1H NMR (400 MHz, CD_3OD,): δ 7.57 (1H, *d*, *J* = 15.9 Hz, H-7), 7.05 (1H, *d*, *J* = 2.0 Hz, H-2), 6.82 (1H, *dd*, *J* = 8.2, 2.0 Hz, H-6), 6.78 (1H, *d*, *J* = 8.2 Hz, H-5), 6.26 (1H, *d*, *J* = 15.9 Hz, H-8), 4.26 (2H, *d*, *J* = 6.0 Hz, H_2-4′), 4.04 (1H, *t*, *J* = 6 Hz, H-3′), 1.47 (3H, *s*, H_3-5′). ^{13}C NMR (100 MHz, CD_3OD): δ 127.9 (C-1), 115.3 (C-2), 146.8 (C-3), 149.6 (C-4), 116.6 (C-5), 123.0 (C-6), 147.2 (C-7), 115.1 (C-8), 169.2 (C=O), 178.0 (C-1′), 74.5 (C-2′), 76.8 (C-3′), 66.0 (C-4′), 23.1 (C-5′).

Hydrolysis of **1**. Compound **1** (3 mg) in 2 N HCl (2 ml) was left for 1 hr at 90°. After neutralization with 1 N NaOH, the soln was concd. The residue was chromatographed on a silica gel column developed with $CHCl_3$–MeOH (9:1), yielding a sugar lactone (0.5 mg). All the data (^1H NMR, IR, and $[\alpha]_D$) of the sugar lactone were identical with those of 2-*C*-methyl-D-erythrono-1,4-lactone described in literature [3,4]. Methyl caffeoate was obtained by alkaline methanolysis with 3% NaOMe.

Preparation of **1** *from* **2**. Compound **2** (2 mg) in 1 M CF_3COOH (1 ml) was left for 1 hr at 70°. After removal of the solvent, ODS CC of the residue with MeOH–H_2O (1:1) gave **1** (0.6 mg) whose data (^1H NMR, IR, MS, $[\alpha]_D$ and TLC) were identical with those of naturally occurring **1**.

Methyl 2-O-*caffeoyl*-2-C-*methyl*-D-*erythronate* (**3**). $[\alpha]_D^{22}$ −6.2° (MeOH; *c* 1.0). EIMS *m/z* (rel. int.): 326 (6), 294 (10), 223 (4), 180 (14), 163 (100), 134 (28). IR ν_{max}^{KBr} cm^{-1}: 3407, 1735, 1698, 1632, 1602, 1524, 1446, 1283, 1164, 1117. ^1H NMR (400 MHz, CD_3OD): δ 7.56 (1H, *d*, *J* = 15.9 Hz, H-7), 7.04 (1H, *d*, *J* = 2.0 Hz, H-2), 6.94 (1H, *dd*, *J* = 8.2, 2.0 Hz, H-6), 6.78 (1H, *d*, *J* = 8.2 Hz, H-5). 6.23 (1H, *d*, *J* = 15.9 Hz, H-8), 4.23 (2H, complex, H_2-4′), 4.02 (1H, complex, H-3′), 3.74 (3H, *s*, OMe), 1.44 (3H, *s*, H_3-5). ^{13}C NMR (100 MHz, CD_3OD): δ 127.8 (C-1), 115.2 (C-2), 146.9 (C-3), 149.7 (C-4), 116.6 (C-5), 123.0 (C-6), 147.3 (C-7), 115.0 (C-8), 169.0 (C=O), 176.6 (C-1′), 74.5 (C-2′), 77.2 (C-3′), 65.8 (C-4′), 22.7 (C-5′), 52.9 (Me).

Methyl 3-O-*caffeoyl*-2-C-*methyl*-D-*erythronate* (**4**). $[\alpha]_D^{22}$ −23.8° (MeOH; *c* 1.0). EIMS *m/z* (rel. int.): 326 (4), 294 (12), 180 (17), 163 (100), 134 (30). IR ν_{max}^{KBr} cm^{-1}: 3416, 1735, 1705, 1635, 1605, 1520, 1450, 1370, 1265, 1160, 1115. ^1H NMR (400 MHz, CD_3OD): δ 7.62 (1H, *d*, *J* = 15.9 Hz, H-7), 7.06 (1H, *d*, *J* = 2.0 Hz, H-2), 6.96 (1H, *dd*, *J* = 8.2, 2.0 Hz, H-6), 6.78 (1H, *d*, *J* = 8.2 Hz, H-5), 6.32 (1H, *d*, *J* = 15.9 Hz, H-8), 5.34 (1H, *dd*, *J* = 5.2 and 6.7 Hz, H-3′), 3.76 (3H, *s*, OMe), 3.74 (2H, complex, H-4′), 1.38 (3H, *s*, H_3-5′). ^{13}C NMR (CD_3OD, 100 MHz): δ 127.8 (C-1), 115.3 (C-2), 146.9 (C-3), 149.7 (C-4), 116.6 (C-5), 123.1 (C-6), 147.6 (C-7), 114.9 (C-8), 168.8 (C=O), 176.0 (C-1′), 76.4 (C-2′), 74.8 (C-3′), 61.5 (C-4′), 23.2 (C-5′), 53.1 (Me).

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