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AN IRIDOID ACETYLALLOSIDE FROM *VIBURNUM JAPONICUM*

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Key Word Index—*Viburnum japonicum*; Caprifoliaceae; iridoid acetylalloside; 2',3'-*O*-diacetylfurcatoside C; furcatoside A; adoxoside; bitter principle.

Abstract—A new iridoid acetylalloside, 2',3'-*O*-diacetylfurcatoside C along with two known iridoid glucosides, furcatoside A and adoxoside, have been isolated from *Viburnum japonicum* and their structures elucidated. The two former compounds are bitter to the taste.

INTRODUCTION

Viburnum japonicum L. is a small evergreen tree found in the Honshu, Kyushu and Ryukyus islands of Japan. Its leaves are very bitter. Earlier studies on the constituents of the plant revealed the presence of chavicol as a *Drosophila* larva-growth inhibitor [1]. However, there has been no previous work on the bitter components. We have examined the leaves of the plant and isolated a new iridoid acetylalloside (**1**) and furcatoside A (**2**) [2] as bitter principles and adoxoside (**3**) [3].

RESULTS AND DISCUSSION

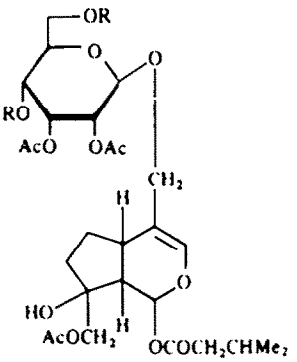
Compound **1** was obtained as a bitter amorphous powder, $[\alpha]_D$ −60.8°, with a molecular formula $C_{27}H_{40}O_{14}\cdot H_2O$. It emitted isovaleric acid on standing and turned black with hydrochloric acid. It showed UV and IR absorptions indicative of a non-conjugated iridoid enol-ether system at 209 nm and at 1655 cm^{-1}, respectively. Its ^1H NMR spectrum showed a doublet at δ6.14 (1H, J = 4 Hz) assignable to an acylated acetal proton at C-1 and a broad singlet at δ6.40 due to an olefinic proton at C-3 along with signals of an isovaleroyl group at δ0.95 (6H, *d*, J = 6 Hz), suggesting that compound **1** was a valeriana iridoid [4]. In addition, signals due to three acetoxyl groups at δ2.03, 2.16 and 2.20 (3H each, *s*) were observed. On acid hydrolysis, compound **1** gave a black polymer and allose which was determined by paper chromatography. Treatment of **1** with acetic anhydride and pyridine afforded a penta-acetate (**4**), $C_{31}H_{44}O_{16}$, whose IR and ^1H NMR spectra were identical with those of furcatoside C acetate [2]. Thus, the position of the isovaleroyl group is located at C-1. The presence of the two acetoxyl groups in the allose moiety was confirmed by the ^1H NMR spectrum of **1**. The signal at δ5.60 (1H, *m*) was characteristic of an acylated proton at C-3 in allose. Irradiation at δ5.60 caused changes in the multiplets at *ca* δ4.2 and 3.88 which were assigned to protons at C-2' and C-4', respectively. These facts showed that the hydroxyl groups at C-2' and C-3' were acetylated because of their low field chemical shifts. The acetylated positions in the allose were further supported by comparison of the ^{13}C NMR spectrum of the sugar parts in **1** with that of 2',3'-*O*-diacetylallose in opulus iridoid I [4] (see Experimental). The remaining acetoxyl group was placed at C-10. The structure of **1** is therefore furcatoside C in which the two hydroxyl groups at C-2' and C-3' are acetylated.

To establish the absolute structure of **1**, it was submitted to acid methanolysis, yielding the methyl acetate (**6**), $C_{11}H_{16}O_4$ and the corresponding monoacetate (**5**), $C_{13}H_{18}O_5$, demonstrating the position of the remaining acetate group at C-10. The ^1H NMR spectrum of **5** indicated the presence of an acetoxyl group at δ2.11 (3H, *s*) and a methoxyl group at δ3.47 (3H, *s*). An AB system at δ4.20 and 4.45 (J = 12 Hz) was due to methylene protons attached to the carbon bearing the acetoxyl group. Signals at δ4.94 and 5.01 (*br s* each), and a doublet at δ5.09 (1H, J = 3 Hz) were attributable to terminal methylene protons and a C-3 proton, respectively. The above data were in agreement with those of 3-acetoxymethyl-8-methoxy-10-methylene-2,9-dioxatricyclo[4.3.1.$0^{3,7}$]decane which had been prepared by methanolysis of furcatosides A–C [2]. The specific rotations and magnitudes of **5** (+77.8°) and **6** (+15°) (lit. +37.5° [2]) were the same as those of other compounds having dioxatricyclo[4.3.1.$0^{3,7}$]decane skeletons [2, 4, 5].

Therefore, the bitter acetylalloside, which we have named 2',3'-*O*-diacetylfurcatoside C, is shown to have the absolute structure **1**. This is the fourth example of iridoid allosides isolated from *Viburnum* species [2, 4, 5].

EXPERIMENTAL

Extraction and isolation. Plant material was collected in Kagoshima city and identified by Dr. S. Sako (Herbarium sample No. 7). Fresh leaves of *V. japonicum* (2.5 kg) were extracted with MeOH (18 l. × 2). The extracts were concentrated, diluted with H_2O and extracted with Et_2O and then EtOAc. The Et_2O extract (25 g) was subjected to CC on silica gel. Elution with $CHCl_3$–MeOH (97:3) gave 2',3'-*O*-diacetylfurcatoside C (**1**, 1.5 g). Furcatoside A (**2**, 226 mg) was obtained from the fractions eluted with $CHCl_3$–MeOH (19:1). The EtOAc extract (23.4 g) was chromatographed on silica gel with $CHCl_3$–MeOH (9:1) to



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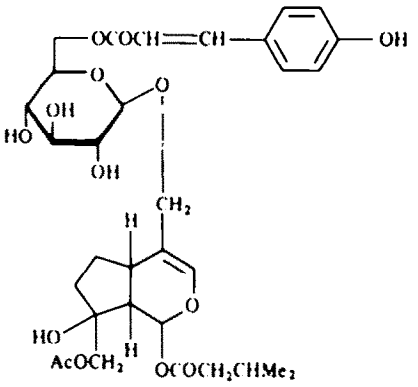
4 R = Ac



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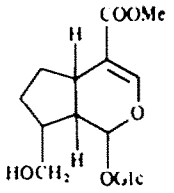

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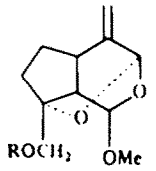

5 R = Ac
6 R = H

afford adoxoside (3) (120 mg). Furcatoside A and adoxoside were identified by comparing their spectral data with those of authentic samples.

2',3'-O-*Diacetylfurcatoside C* (1). A bitter amorphous powder; $[\alpha]_D$ −60.8° (MeOH; *c* 0.185); UV λ_{max}^{MeOH} nm (ε): 209 (3700); IR ν_{max}^{film} cm^{-1}: 3450, 1740, 1665, 1145, 1090, 1040; ^{1}H NMR (100 MHz, $CDCl_3$): δ0.95 (6H, *d*, *J* = 6 Hz, isovaleroyl Me groups), 2.03, 2.16 and 2.20 (3H each, *s*, OAc), 3.88 (3H, *m*, H-4' and H-6'), 4.16 (2H, *s*, H-11), 4.20–4.36 (2H, *m*, H-1' and H-2'), 4.83 (2H, *s*, H-10), 5.60 (1H, *m*, H-3'), 6.18 (1H, *d*, *J* = 4 Hz, H-1), 6.40 (1H, *s* (*br*), H-3); ^{13}C NMR (25.05 Hz, $CDCl_3$): δ20.8 ($MeCOO \times 3$), 22.3, 25.7 and 43.4 (Me_2CHCH_2COO), 28.4 (C-6), 35.1 (C-5), 37.5 (C-7), 45.8 (C-9), 62.4 (C-6'), 66.6 (C-4'), 68.9 (C-11), 70.0 (C-10), 70.8 (C-2), 71.3 (C-3'), 74.0 (C-5'), 80.3 (C-8), 89.8 (C-1), 97.4 (C-1'), 113.3 (C-4), 140.1 (C-3), 169.6, 171.0, 171.3 and 171.5 ($COO \times 4$); MS *m/z* (rel. int.): no [M]$^+$, 331 (0.9), 247 (0.7), 222 (4), 180 (25), 134 (100), 85 (96). (Found: C, 53.20; H, 6.72%. Calc. for $C_{27}H_{40}O_{14} \cdot H_2O$: C, 53.48; H, 6.93%.) Compound 1 (7 mg) was hydrolysed by refluxing with 2 M HCl (0.5 ml) for 4 hr. The resulting black precipitate was filtered off and the aq. soln was neutralized with Amberlite IRA-45 (10 g). The presence of allose in the resiude was confirmed by co-PC (solvent system: EtOAc–pyridine–H_2O–HOAc, 5:5:3:1).

Acetylation of 1. A soln of 1 (41 mg) in Ac_2O and C_5H_5N was allowed to stand at room temp. The crude product was chromatographed on silica gel with $CHCl_3$–MeOH (99:1) to give an amorphous powder 4 (41 mg): IR ν_{max}^{film} cm^{-1}: 3500, 1745, 1665, 1225, 1100, 1040, ^{1}H NMR (100 MHz $CDCl_3$): δ0.95, (6H, *d*, *J* = 6 Hz), isovaleroyl Me groups), 1.99 (6H, *s*, OAc), 2.06, 2.11 and 2.16 (3H each, *s*, OAc), 4.03 and 4.82 (2H each, *s*, H-11 and H-10), 5.62 (1H, *m*, H-3'), 6.20 (1H, *d*, *J* = 4 Hz, H-1), 6.38 (1H, *s* (*br*), H-3). (Found: C, 55.75; H, 6.65%. Calc. for $C_{31}H_{44}O_{16}$: C, 55.35; H, 6.59%.)

Methanolysis of 1. To a soln of 1 (50 mg) in dry MeOH (1 ml), was added a catalytic amount of conc. HCl and the mixture was stirred at 50° for 30 min under N_2. The reaction mixture was diluted with H_2O, extracted with EtO_2 and washed with H_2O and brine. CC of the crude product on silica gel with $CHCl_3$–hexane (1:1) gave a mono-acetate (5, 2.7 mg) and an alcohol (6, 2 mg). Compound 5, an oil; $[\alpha]_D$ +77.8° ($CHCl_3$; *c* 0.135); IR ν_{max}^{film} cm^{-1}: 1740, 1660, 1220, 1070, 950; ^{1}H NMR (100 MHz, $CDCl_3$): δ2.11 (3H, *s*, OAc), 3.47 (3H, *s*, OMe), 4.20 and 4.45 (AB, *J* = 12 Hz, H-11), 4.94 and 5.01 (1H, each, *s* (*br*), H-10), 5.09 (1H, *d*, *J* = 3 Hz, H-8), 5.16 (1H *s* (*br*), H-1). (Found: *m/z* 254.1169. Calc. for $C_{13}H_{18}O_5$: *m/z* 254.1154.) Compound 6, an oil; $[\alpha]_D$ +15° ($CHCl_3$; *c* 0.1); IR ν_{max}^{film} cm^{-1}: 3450, 1660, 1120, 1060, 960; ^{1}H NMR (100 MHz, $CDCl_3$): δ3.44 (3H, *s*, OMe), 4.94 and 5.02 (1H each, *s* (*br*), H-11), 5.20 (1H, *s*, H-3), 5.27 (1H, *d*, J = 2 Hz, H-8). (Found: *m/z* 212.1008. Calc. for $C_{11}H_{16}O_4$: *m/z* 212.1048.)

Furcatoside A (2). A bitter amorphous powder; IR ν_{max}^{film} cm^{-1}: 3400, 1630, 1600, 1580, 1510, 830; ^{1}H NMR (100 MHz, Me_2CO-d_6): δ0.93 (6H, *d*, *J* = 6 Hz, isovaleroyl Me groups), 2.00 (3H, *s*, OAc), 5.10 (1H, *d*, *J* = 8 Hz, H-1'), 6.17 (1H, *d*, *J* = 6 Hz, H-1), 6.46 (1H, *s* (*br*), H-3), 6.42 and 7.80 (AB, *J* = 16 Hz, –CH=CH–), 6.98 and 7.62 (AA, BB, *J* = 8 Hz, Ar–H).

Adoxoside (3). An amorphous powder; $[\alpha]_D$ −49.3° (MeOH; *c* 0.487); UV λ_{max}^{MeOH} nm (ε): 236 (8500); IR ν_{max}^{film} cm^{-1}: 3400, 1690, 1620; ^{1}H NMR (200 MHz, CD_3OD): δ3.70 (3H, *s*, COOMe), 4.66 (1H, *d*, *J* = 8 Hz, H-1'), 5.17 (1H, *d*, *J* = 6 Hz, H-1), 7.46 (1H, *d*-like *J* = 1 Hz, H-3). (Found: C, 51.32; H, 6.86%. Calc. for $C_{17}H_{26}O_{10} \cdot 1.2\,H_2O$: C, 51.12; H, 6.81%.) Acetylation of 3 gave needles from EtOH, mp 140.5–141.5°; IR ν_{max}^{film} cm^{-1}: 1750, 1710, 1630; ^{1}H NMR (100 MHz, $CDCl_3$): δ1.94, 2.00, 2.04, 2.07 and 2.09 (3H each, *s*, OAc), 3.72 (3H, *s*, COOMe), 4.05 (2H, *d*, *J* = 6 Hz, H-10), 7.40 (1H, *s* (*br*), H-3).

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GERMACRANOLIDES FROM *ANVILLEA GARCINI*

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Key Word Index— *Anvillea garcini*; Compositae; sesquiterpene lactones; germacranolides.

Abstract—The aerial parts of *Anvillea garcini* afforded three germacranolides, two of which had not being isolated previously. The structures were elucidated by ^{1}H NMR spectroscopy. The configuration of 9-acetoxy parthenolide at C-9 has been revised.

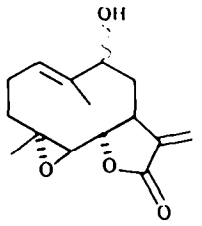
INTRODUCTION

The small genus *Anvillea* (tribe Inuleae, subtribe Inulinae) is placed in the Inula group [1]. From *A. garcini* (Burm.) DC flavones [2] and 9α-hydroxyparthenolide (**1**) [3] were reported. A reinvestigation of a sample collected in the South of Iran gave in addition to 9α-hydroxyparthenolide (**1**), two further lactones, **2** (the epimer of **1**) and **3** (the epoxide of **2**). The structures were elucidated by high field ^{1}H NMR spectroscopy.

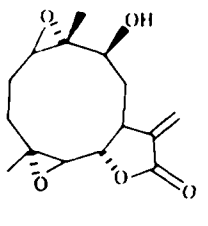
RESULTS AND DISCUSSION

The spectrum of **2** (Table 1) was in part close to that of **1**, apart from the H-9 signal which showed a very different splitting pattern. Spin decoupling allowed the assignment of all signals. Irradiation of the five-fold doublet at δ2.86 collapsed the H-13 doublets to singlets and therefore were due to H-7. The latter was further coupled with three-fold doublets at δ2.11 and 2.01. As the corresponding protons were further coupled with the double doublet at δ4.27 (H-9) and H-7 also was coupled with the triplet at δ3.86 (H-6), which itself collapsed to a doublet on irradiation of the doublet at δ2.69 (H-5) the whole sequence H-5–H-9 was settled. The signals of H-1–H-3 were nearly identical with those of **1**, accordingly, the structure and the stereochemistry of **2** were settled and the structure of a lactone from *Matricaria suffruticosa* which was errously given as the acetate of **2** [4] has to be revised to 9α-acetoxyparthenolide, the acetate of **1** as the couplings of H-9 are small.

The ^{1}H NMR spectrum of **3** (Table 1) indicated that this lactone had no olefinic double bonds. Spin decoupling allowed the assignment of all signals though a few were overlapping multiplets. A multiplet at δ2.83 (H-7) was coupled with the doublets at δ6.38 and 5.70 as well as with the triplet at δ3.94 (H-6), the threefold doublet at δ1.89 (H-8) and the multiplet at δ2.28 (H-8). A double doublet at δ3.28 was coupled with H-8 and therefore was due to H-9.



1 9α OH
2 9β OH



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