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PHENOLIC CONSTITUENTS OF *VIBURNUM CARLESII*

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Abstract

Three phenolic glycosides, arbutin (4-hydroxyphenyl β-D-glucopyranoside), 6-*O*-*p*-coumarylabutin and 6-*O*-cafferylarbutin and have been isolated from the methanolic extract of the leaves of *Viburnum carlesii*. The chemotaxonomic relationship between *Viburnum* and Proteaceae is briefly discussed.

Introduction

Deciduous shrub *Viburnum carleii* (Caprifoliaceae) (Japanese name : Choujigamazumi) grows in the temperate zone of Japan and Korea. In a continuation of the investigation on phenolic constituents of the genus *Viburnum*[1-4] the methanolic extract of the leaves of *V. carlesii* was examined to yield three phenolic glucosides **1**, **2** and **3**. Fig. 1 showed the isolation procedure of the compounds.

Results and discussion

Compounds (**1**) was crystallized as prisms, mp 206-207.5° with a molecular formula $C_{12}H_{16}O_7$. The IR spectrum showed absorption bands for a hydroxyl group at 3350 cm^{-1} and a *p*-substituted phenyl group at 1610, 1520 and 835 cm^{-1}. The presence of the *p*-substituted phenyl group was also confirmed by signals at δ 6.65 and 6.98 (A_2B_2, $J=8$ Hz) in the ^1H NMR spectrum. Signals due to sugar protons appeared at δ 3.26-3.46 (3H, *m*), 3.61 (1H, *dd*, $J=4$ and 12 Hz, H-6′), 3.85 (1H, *br d*, $J=12$ Hz, H-6′) together with a doublet of an anomeric proton at δ 4.77 ($J=8$ Hz). On acetylation with acetic anhydride and pyridine, compound **1** gave a penta-acetate (**4**), mp 150-151° with a molecular formula $C_{22}H_{26}O_{12}$. The ^1H NMR spectrum of the acetate indicated the presence of four alcoholic acetoxyl groups at δ 2.04-2.08 (3H x 4, *s*) and one phenolic acetoxyl group at δ 2.29 (3H, *s*). The above results suggested that compound **1** was arbutin (*p*-hydroxyl β-D-glucopyranoside). Its identity as arbutin was established by comparing its spectropscopic data and physical properties with those of an authentic sample.

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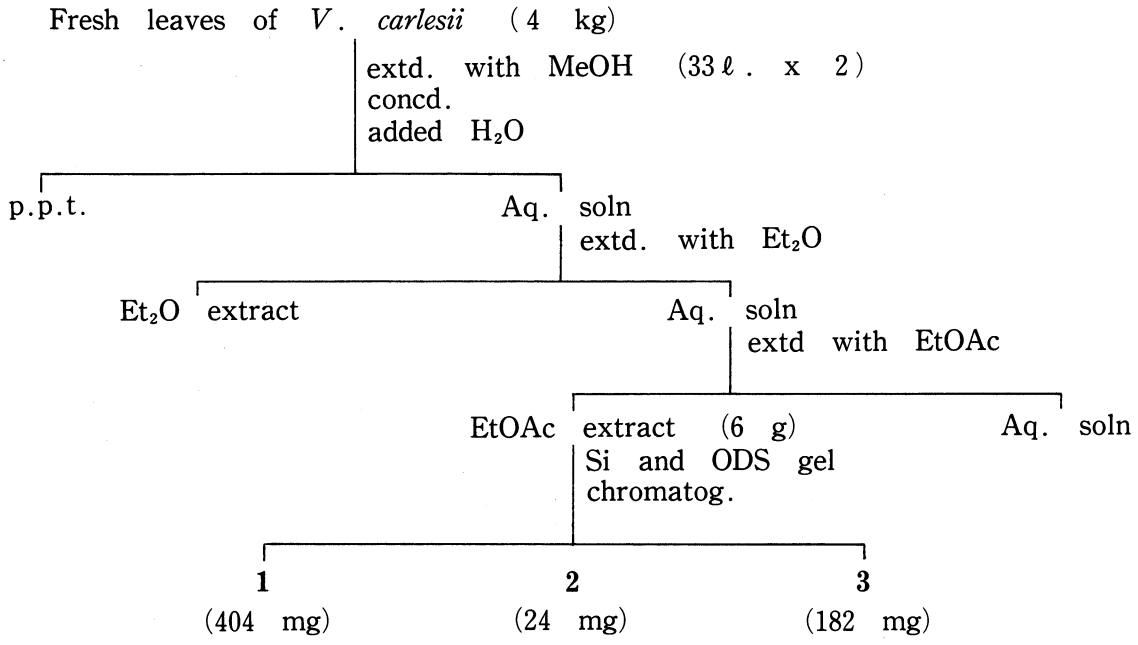


Fig. 1. Isolation procedure of the compounds

Compound (**2**) was isolated as needles, mp 214-215° with a molecular formula $C_{21}H_{22}O_{10} \cdot 1.8H_2O$. The IR spectrum showed the presence of a hydroxyl group at 3300 cm^{-1}, an α, β-unsaturataed ester carbonyl group at 1685 cm^{-1} and a *p*-substitutd phenyl group at 1605, 1590, 1510 and 830 cm^{-1}. The ^1H NMR spectrum was similar to that of **1** except for additional signals due to a *p*-coumaroyl group at δ 6.34 and 7.63 (AX, *d*, $J=16$ Hz) and δ 6.82 and 7.45 (A_2B_2, *d*, $J=8$ Hz). Compound **2** was acetylated with acetic anhydride and pyridine to give a penta-acetate (**5**), mp 196-197° with a molecular formula $C_{31}H_{32}O_{14}$. The ^1H NMR spectrum of the acetate showed signals at δ 2.04-2.07 (3H x 3, *s*) due to three alcoholic acetoxyl groups together with silgnals at δ 2.26 and 2.32 (3H each, *s*) arising from two phenolic acetoxyl groups. On the basis of the above results **2** was assumed to be a *p*-coumaric ester of arbutin. To confirm this assumption, compound **2** was hydrolyzed to provide *p*-coumaric acid and arbutin whose IR spectra were identical wilth those of authenic samples. The ^1H NMR spectrum of **2** also showed that the ester linkage was located at C-6 of glucose. Signals at δ 4.34 (1H, *dd*, $J=6$ and 12 Hz) and δ 4.54 (1H, *dd*, $J=2$ and 12 Hz) due to H-6′ were shifted downfield by 0.73 and 0.69 ppm, respectively, compared with those of **1**. Furthermore, it was supported by the ^{13}C NMR spectrum (Table 1). A signal for C-6′ appeared downfield by 1.9 ppm, compared with that of 1. Compound **2** therefore should be 6-*O*-*p*-coumarylarbutin[5].

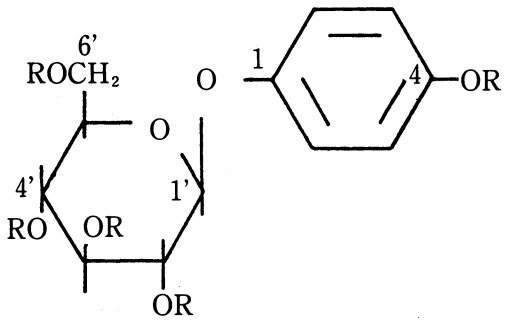
Compound (**3**) was obtained as needles, mp 215-217° with a molecular formula,

Tabale 1. ^{13}C NMR spectral data of **1**, **2**, and **3**[a)]

Carbon No.	1	2	3
1	153.8	153.8	153.9
2	116.7	116.6 b)	116.7
3	119.5	119.6	119.7
4	152.4	152.1	152.4
5	119.5	119.6	119.7
6	116.7	116.6 b)	116.7
1'	103.7	103.7	103.8
2'	75.5	74.8	75.0
3'	78.1	77.8	78.0
4'	71.5	71.7	71.9
5'	78.1	75.4	75.6
6'	62.7	64.6	64.7
COO		166.8	169.0
α-C		146.7	147.2 d)
β-C		114.9	115.0
1"		127.0	127.8
2"		131.0	116.7 d)
3"		116.8 c)	146.8
4"		161.1	149.6
5"		116.8 c)	115.0
6"		131.0	123.1

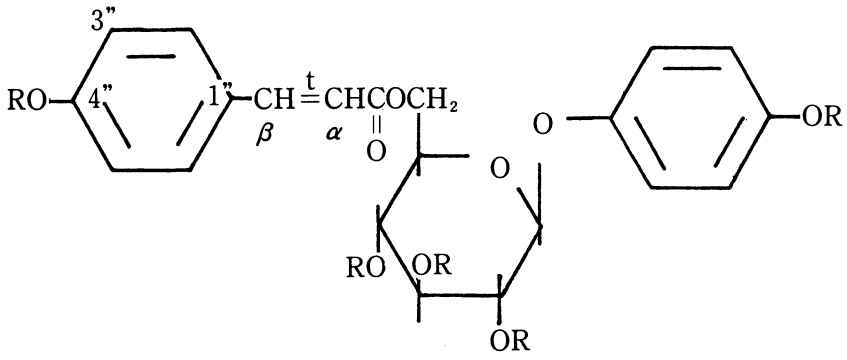
a) 50.10 MHz, in CD_3OD with TMS as internal reference
b), c), d) These values may be interchangeble in the vertical column.

$C_{21}H_{22}O_{10} \cdot H_2O$. The IR spectrum contained absorption bands of a hydroxyl group at 3350 cm^{-1}, an α,β-unsaturated ester carbonyl group at 1690 and 1630 cm^{-1}, a *p*-substituted phenyl group at 1600 and 830 cm^{-1}. The ^1H NMR specturm was very similar to that of **2** except for singals arising from aromatic protons in the α,β-unsaturated ester moiety. One ABX pattern at δ 6.66 (1H, *br d*, $J=9$ Hz), 6.96 (1 H, *br d*, $J=9$ Hz) and 7.06 (1H, *br d*, $J=2$ Hz) together with one AX pattern at δ 6.30 and 7.58 (1H each, *d*, $J=6$ Hz) showed the presence of a cafferoyl group in **3**. Acetylation of **3** with acetic anhydride and pyridine gave a hepta-acaetate (**6**), mp 180-181° with a molecular formula $C_{33}H_{34}O_{16} \cdot 1/2H_2O$. The ^1H NMR sepctrum of the latter showed signals for three alcoholic acetoxyl groups at δ 2.04-2.07 (3H x 3, *s*) and for three phenolic acetoxyl groups at δ 2.26-2.32 (3H x 3, *s*) . The



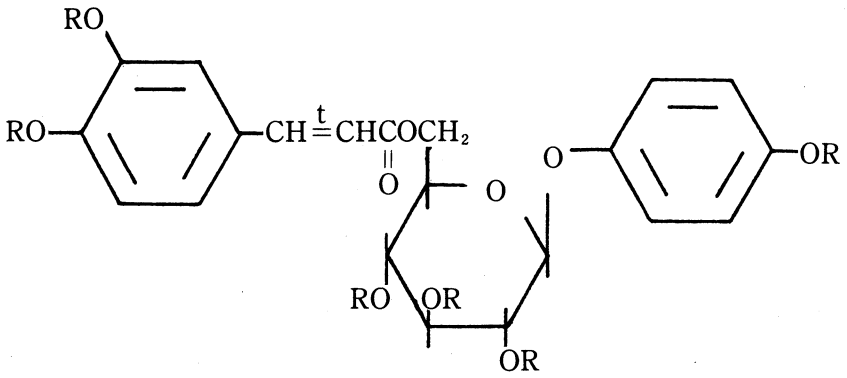
1 R=H

4 R=Ac



2 R=H

5 R=Ac



3 R=H

6 R=Ac

above data suggested that compond **3** was a cafferic ester of arbutin. The ester linkage was located at C-6′ of glucose, since signals due to H-6′ was shifted downfield by about 0.71 ppm, as compared with those of **1**. The proposed structure was also in accordance with the data of the ^{13}C NMR spectrum. A signal at δ 64. 7 in **3** was deshielded by 2 ppm, as compared with that of **1**. Compound **3** therefore must be 6-*O*-caffeylarbutin[5-6] .

Although 6-*O*-*p*-coumarylarbutin was isolated as a new compound from *Grevilla robusta* (Proteaceae), the physical data (mp, $[\alpha]_D$and ^1H NMR) were not correct or not measured [5] . Furthermore, in case of 6-*O*-cafferylarbutin and the acetate the physical date were also uncorrect and incomplete [5-6]. Their structures, howeves,. were assured by the above results. Arbutin derivtives, a spiro -bis lactone glucoside [3] which was very rare, and a phenolic alloside [4] have been isolated from *Viburnum* species. From Proteaceae [3 and 7] the glycosides of the same type as the above compounds also have been obtained. Therefore the relationship between *Viburnum* and Proteaceae may be close.

Experimental

Extraction and isolation. Plant material was collected in Niimi city, Okayama prefecture and identified by Dr. S. Sako. The fresh leaves of *V. carlesii* (4 kg) were extracted with MeOH (33 ℓ . x 2). After concentration of the combined MeOH solns, H_2O was added and the insoluble material filtered off. The filtrate was extraced continusly with Et_2O and then EtOAc. The EtOAc extract was evaporated to give a residue (6 g), which was subjected to a silica gel column with $CHCl_3$-MeOH with increasing proportions of MeOH. The fractions eluted with $CHCl_3$-MeOH (85 : 15) were further applied to a column of ODS gel with H_2O-MeOH (40 : 60) gave **2** (24 mg) and **3** (182 mg). Elution with $CHCl_3$-MeOH (80 : 20) afforded **1** (404 mg).

Arbutin **1**. Prisms from Me_2CO, mp 206.5-207°, $[\alpha]_D$-63.6° (MeOH; *c* 0.11);UV λ_{max}^{MeOH} nm (ε) : 213 (6500), 285 (1960); IR ν_{max}^{Nujol} cm^{-1} : 3350, 1610, 1520, 900, 835, 780 ; ^1H NMR (200 MHz, CD_3OD):δ 3.26-3.46 (3H, *m*, sugar H), 3.61 (1H, *dd*, J=4 and 12 Hz, H'-6), 3.85 (1H, *br d*, J=12 Hz,H-6′), 4.77 (1H, *d*, J=8 Hz, H-1′), 6.65 and 6.98 (A_2B_2, J=8 Hz, H-2 and H-6, and H-3 and H-5). (Found : C, 52.65 ; H, 5. 93%. Calc. for $C_{12}H_{16}O_7$: C, 52.93 ; H, 5.92%.) Compound **1** (40 mg) was acetylated with Ac_2O and pyridine to give **4** (33 mg), needles from EtOH-CH_2Cl_2, mp 150-151° , IR ν_{max}^{Nujol} cm^{-1} : 1750, 1605, 1595, 1500, 900, 860, 830, 710 ; ^1H NMR (400 MHz, $CDCl_3$): δ 2.04, 2.05, 2.06, 2.08, 2.29 (3H each, *s*), 3.84 (1H, *m*), 4.17 (1H, *dd*, J=2 and 13 Hz), 4.29 (1H, *dd*, J=5 and 13 Hz), 5.34 (1H, *d*, J=8 Hz), 5.14-5.31 (3H, *m*), 7. 00 (4H, *s*). (Found : C, 54. 78 ; H, 5.43%. Calc. for $C_{22}H_{26}O_{12}$: C, 54. 77 ; H, 5. 43%.)

6-*O*-*p*-*Coumarylarbutin* **2**. Needles from MeOH-$CHCl_3$, mp 214-215° (lit. [5] mp 64-65°), $[\alpha]_D$-68.1° (MeOH, *c*, 0.075); UV λ_{max}^{MeOH} nm (ε) : 226 (14700), 300 (18700), 314 (20200); IR ν_{max}^{Nujol} cm^{-1} : 3300, 1685, 1605, 1590, 1510, 975, 830, 780 ; ^1H NMR (200

MHz, CD_3OD): δ 3.2-3.7 (3H, *m*, sugar H), 4.34 (1H, *dd*, J=6 and 12 Hz, H-6′), 4.54 (1H, *dd*, J=2 and 12 Hz, H-6′), 4.72 (1H, *d*, J=7 Hz, H-1′), 6.34 and 7.63 (AX, J=16 Hz, α-and β-H), 6.65 and 6.95 (A_2B_2, J=8 Hz, H-2 and H-6, and H-3 and H-5), 6.82 and 7.45 (A_2B_2, J=8 Hz, H″-2 and H-6″, and H-3″ and H-5″); FAB MS *m/z*: 419 $[M+1]^+$. (Found: C, 55.93; H, 5.63%. Calc. for $C_{21}H_{22}O_{10}\cdot 1.8H_2O$: C, 55.96; H, 5.69%.) Compound **2** (49 mg) was treated with Ac_2O and pyridine to yield (30 mg), needles from EtOH, mp 196-197° (lit. [2] mp 194-195), IR ν_{max}^{Nujol} cm^{-1}: 1755, 1720, 1630, 1600, 1500, 910, 830; ^1H NMR (400 MHz, $CDCl_3$): δ 2.04, 2.06, 2.07, 2.26, 2.32 (3H each, *s*), 4.34 (1H, *dd*, J=5 and 12 Hz), 4.40 (1H, *dd*, J=3 and 12 Hz), 5.06 (1H, *d*, J=7 Hz), 5.18-5.31 (3H, *m*), 6.40 and 7.68 (AX, J=16 Hz), 6.95-7.01 (A_2B_2-like, J=9 Hz), 7.14 and 7.55 (A_2B_2, J=9 Hz). (Found: C, 59.19; H, 5.11%. Calc. for $C_{31}H_{32}O_{14}$: C, 59.23; H, 5.13%.) Compound **2** (82 mg) was dissolved in MeOH (1 ml) and 1N NaOH (1 ml). The mixture was stirred under N_2 overnight at r.t. The reaction mixture was neutralized with 1N HCl and evaporated. CC of the crude product on Si gel with $CHCl_3$-MeOH (95 : 5) to afford *p*-coumaric acid (14 mg), prisms from MeOH-H_2O, mp 216-217°; IR ν_{max}^{Nujol} cm^{-1}: 3400, 1670, 1605, 1590, 1510, 980, 835. The IR spectrum was identical with that of *p*-coumaric acid. Further elution with $CHCl_3$-MeOH (90 : 10) gave arbutin (5 mg), prisms from MeOH-$CHCl_3$, mp 206-207°; IR ν_{max}^{Nujol} cm^{-1}: 3300, 1510, 830. The IR spectrum was in good agreement with that of arbutin.

6-*O*-*Caffeylarbutin* **3**. Needles form H_2O-MeOH, mp 215-217° (lit. [5-6], the mp was not measured.), $[\alpha]_D$-51.7° (MeOH, *c*, 0.097); UV λ_{max}^{MeOH} nm (ε): 220 (16800), 250 (7060), 295 (13200), 340 (15900); IR ν_{max}^{Nujol} cm^{-1}: 3350, 1690, 1630, 1600, 830, 780; ^1H NMR (200 MHz, CD_3OD): δ 3.36-3.72 (3H, *m*, sugar H), 4.35 (1H, *dd*, J=6 and 12 Hz, H-6′), 4.53 (1H, *dd*, J=2 and 12 Hz, H-6′), 4.74 (1H, *d*, J=7 Hz, H-1′), 6.30 and 7.58 (AX, J=16 Hz, α-and β-H), 6.66 (1H, *d*, J=9 Hz, H-5″), 6.96 (1H, *br d*, J=9 Hz, H-6″) and 7.06 (1H, *br d*, J=2 Hz, H-2″); FAB MS *m/z*: 435 $[M+1]^+$. (Found: C, 55.62; H, 5.74%. Calc. for $C_{21}H_{22}O_{10}\cdot H_2O$: C, 55.74; H, 5.35%.) Acetylation of **3** (47 mg) with Ac_2O and pyridine gave **6** (35 mg), needles form EtOH-CH_2Cl_2 mp 180-181° (lit. [5] mp 86-87°, lit. [6] mp 134 and 270); IR ν_{max}^{Nujol} cm^{-1}: 1765, 1720, 1645, 910, 840; ^1H NMR (400 MHz, $CDCl_3$): 2.04, 2.06, 2.07, 2.26, 2.31, 2.32 (3H each, *s*), 3.90-3.94 (1H, *m*),4.35 (1H, *dd*, J=5 and 12 Hz), 4.39 (1H, *dd*, J=3 and 12 Hz), 5.05 (1H, *d*, J=7 Hz), 5.17-5.31 (3H, *m*), 6.39 and 7.64 (AX, J=16 Hz), 6.95-7.01 (AB-like, J=9 Hz), 7.24 (1H, *d*, J=8 Hz), 7.37 (1H, *d*, J=2 Hz), 7.41 (1H, *dd*, J=2 and 8 Hz). (Found: C, 57.07; H, 4.77%. Calc. for $C_{33}H_{34}O_{16}\cdot 1/2H_2O$: C, 56.98; H, 5.07%.)

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