The Revised Structure of Furcation, a Component of Leaves of *Viburnum furcatum* Blume

Tsunao HASE* and Tetsuo IWAGAWA

Department of Chemistry, Faculty of Science, Kagoshima University, Korimoto, Kagoshima 890

(Received April 26, 1982)

Synopsis. The structure of furcatin, which was proposed to be *p*-vinylphenyl 6-*O*-apiosyl-(1→6)-*β*-D-glucoside, was revised to *p*-allylphenyl 6-*O*-[3-*C*-(hydroxymethyl)-*β*-D-erythrofuranosyl]-(1→6)-*β*-D-glucopyranoside by spectral and chemical results.

The structure of furcatin was reported to be phenolic glycoside (**1**) isolated as a source of bitterness from *Viburnum furcatum* Blume.[1] Its aglycone was determined as *p*-vinylphenol based on the fact that the methylated aglycone could be oxidized with permanganate, Beckmann mixture, and ozone to give *p*-methoxybenzoic acid, *p*-methoxybenzaldehyde, and formaldehyde, respectively.

However, purified furcatin was not bitter. Spectral and chemical results show that the structure should be revised to *p*-allylphenyl glycoside (**2**).

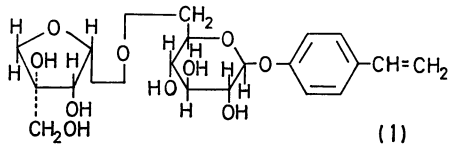
2, colorless needles, mp 160.5—161.5 °C, $[\alpha]_D^{20}$ −103.5; these were identical with results from an authentic sample previously isolated by Hattori and Imaseki. It has a molecular formula $C_{20}H_{28}O_{10}$ and the spectral data showed the presence of a *p*-substituted allylbenzene ring [$\nu_{C=C}$ 1640, 1610, 1590, 1510, 995, 960, 910, and 825 cm^{-1}; λ_{max} 213, 222, 273, and 279 nm; δ 3.27 (2H, d), 4.99 (1H, bd), 5.02 (1H, bd), 6.00 (1H, m), 7.25, and 7.51 (2H each, A_2B_2).

Acetylation of **2** with acetic anhydride and pyridine gave an amorphous powder (**3**), $C_{32}H_{40}O_{16}$, whose NMR spectrum showed the signals for six acetyl groups δ 2.00—2.07 (3H×6). Treatment of **2** with 2 M (1 M=1 mol dm^{-3}) sulfuric acid afforded an aglycone (**4**) and two sugars which were identified as D-glucose and D-apiose by paper chromatography. The spectra of the aglycone **4** were identical with those of an authentic sample of *p*-allylphenol.[2]

2 was methylated with sodium hydride, dimethyl sulfoxide, and methyl iodide, giving hexamethyl ether (**5**) [*m/z* 512 (M^+); δ 1.83 (3H, d, J=6 Hz) and 3.34—3.62 (3H×6, s)], which seemed to suffer an allylic rearrangement during methylation. Upon hydrolysis with hydrochloric acid, **5** yielded *p*-(1-propenyl)phenol, 2,3,4-tri-*O*-methyl-D-glucose, and 2,3,3′-tri-*O*-methyl-D-apiose. The methylated D-apiose was identified by direct comparison with an authentic sample obtained from heptamethylapiin.[3] Therefore, the structure of apiose in **2** should be 3-*C*-(hydroxymethyl)-D-erythrofuranose.

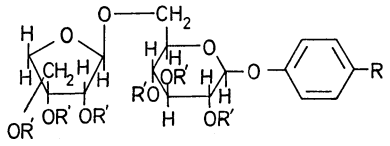
A *β*-glucosidic linkage in **2** was inferred from the anomeric proton signal at δ 5.50 (1H, m, $W_{1/2}$=10 Hz) in the NMR spectrum of **2**. Upon partial hydrolysis with ion exchange resin, **2** gave a glucoside which was determined to be *p*-allylphenyl *β*-D-glucoside (**6**); its negative molecular rotation was consistent with the existence of a *β*-glucosidic linking in **2**.

A *β*-glycosidic linkage of D-apiose to D-glucose was deduced by applying Klyne's rule. The difference of the molecular rotation between **2** (−441°) and **6** (−180°) was −261°, suggesting that the anomeric configuration of D-apiose in **2** is *β*.[3]

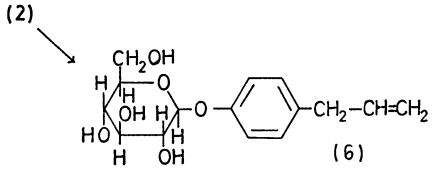


(1)

Configuration shown by dotted lines has not been elucidated.[1]



(2) R: CH_2–CH=CH_2, R′: H
(3) R: CH_2–CH=CH_2, R′: CH_3CO
(5) R: CH=CH–CH_3, R′: CH_3



(6)

The above data show that the structure of furcatin **2** is *p*-allylphenyl 6-*O*-[3-*C*-(hydroxymethyl)-*β*-D-erythrofuranosyl]-(1→6)-*β*-D-glucopyranoside.

Only two *p*-allylphenol diglycosides, rutinoside[4] and 4-*O*-*α*-L-arabinofuranosyl-(1→4)-*β*-D-glucopyranoside[5] have so far been isolated; furcatin is the third example.

Experimental

The plants were collected in the northern highlands of Kagoshima prefecture. All the melting points were uncorrected. IR and UV spectra were taken on a Shimadzu IR-27 and a Shimadzu UV-210A spectrophotometers, respectively. ^{1}H-NMR spectra were obtained on a JEOL MH-100 spectrometer; the chemical shifts are given in δ-values with respect to TMS as the internal standard. Mass spectra were taken on a JEOL D-300 mass spectrometer. The optical rotations were measured on a Nihonbunko J-20 recording spectropolarimeter.

Isolation. The fresh leaves of *V. furcatum* Blume (480 g) were extracted with methanol (4 l×2). The extracts were evaporated to dryness *in vacuo* to give a residue (75 g), which was dissolved in water and extracted with ether and then ethyl acetate.

The ethyl acetate extract (8 g) was subjected to chromatography on a silica-gel column with methanol–chloroform (1:9 v/v) and recrystallized from ethyl acetate saturated with water to give furcatin **2**, needles, (500 mg), mp 160—

161.5 °C, $[\alpha]_D^{20}$ −103.5 (*c*, 0.575, MeOH); λ_{max}^{MeOH} nm (*ε*): 213 (9900), 222 (11000), 273 (1300), and 279 (990); ν_{max}^{Nujol} cm^{-1}: 3350, 1640, 1610, 1590, 1510, 995, 910, and 825; ^1H NMR (pyridine-d_5): *δ* 3.27 (2H, d, *J*=7 Hz, $C\underline{H}_2$–C=C), 4.99 (1H, bd, *J*=12 Hz, H\C=C(H)/H), 5.02 (1H, bd, *J*=15 Hz, H\C=C(H)/H), 5.50 (1H, m, $W_{1/2}$=10 Hz), 5.75 (1H, d, *J*=2 Hz), 6.00 (1H, m, $-CH_2-C\underline{H}=CH_2$), 7.25, and 7.51 (2H each, A_2B_2, *J*=9 Hz, aromatic H). Found: C, 55.64; H, 6.62%. Calcd for $C_{20}H_{28}O_{10}\cdot\frac{1}{4}H_2O$: C, 55.48; H, 6.64%.

Acetylation of **2**. **2** (100 mg) was treated with pyridine–acetic anhydride (1:1 2 ml) at room temperature. The product was chromatographed on a silica-gel column with methanol–chloroform (1:99 v/v) to give an amorphous hexaacetate **3** (100 mg); ν_{max}^{Nujol} cm^{-1} (no OH absorption) 1750, 1640, 1590, 910, and 830; ^1H NMR ($CDCl_3$): 2.0—2.07 (3H×6, s, $COC\underline{H}_3$), 3.31 (2H, d, *J*=6 Hz, $-C\underline{H}_2-CH=C$), 6.86 and 7.06 (2H each, A_2B_2, *J*=8 Hz, aromatic H); MS *m/z* 620 (M^+-60). Found: C, 56.48; H, 6.03%. Calcd for $C_{32}H_{40}O_{16}$: C, 56.46; H, 5.92%.

Hydrolysis of **2** *with Sulfuric Acid.* **2** (100 mg) was dissolved in 2 M sulfuric acid (2 ml) and the solution was stirred at 80 °C for 1 h. The reaction mixture was diluted with water, extracted with ether, washed with water and dried over Na_2SO_4. The solvent was evaporated to give an oily aglycone **4** (25 mg), ν_{max}^{film} cm^{-1}: 3300, 1640, 1610, 1600, 1510, 995, 915, and 820; ^1H NMR ($CDCl_3$): 3.33 (2H, d, *J*=6 Hz, $-C\underline{H}_2-CH=C$), 4.83—5.12 (2H, bd, $-CH=C\underline{H}_2$), 5.67—6.36 (1H, m, $-CH_2-C\underline{H}=CH_2$), 6.80, and 7.14 (2H each, A_2B_2, *J*=9 Hz). These data were identical with those of an authentic *p*-allylphenol.[2] The aqueous solution was neutralized with an excess of barium carbonate, then the precipitate was filtered off and the filtrate was evaporated to dryness *in vacuo*. The paper chromatography of the product showed the presence of D-apiose and D-glucose [solvent system, AcOEt:pyridine:H_2O:AcOH=5:5:3:1].

Methylation of **2**. A solution of sodium hydride (250 mg) in dimethyl sulfoxide (5 ml) was stirred at 70 °C for 1 h under an atmosphere of nitrogen. After cooling to room temperature, a solution of **2** (100 mg) in dimethyl sulfoxide (2 ml) was added to the solution. After the mixture was stirred for 1 h, methyl iodide (1 ml) was added to it. The reaction mixture was stirred for 4 more hours, then poured into ice water and extracted with chloroform. The extract was washed with water and dried over Na_2SO_4 and the solvent was evaporated to give a crude product which was chromatographed on silica gel with methanol–chloroform (1:99 v/v) to give an oily permethylate **5** (100 mg), ν_{max}^{film} cm^{-1}: (no OH absorption) 1610, 1580, 1510, 990, 960, 840, and 790; ^1H NMR ($CDCl_3$): 1.83 (3H, d, *J*=6 Hz, $-C=C(H)(C\underline{H}_3)$), 3.34, 3.46, 3.52, 3.62 (total 3H×6, s, $OC\underline{H}_3$), 6.92, and 7.20 (each 2H, A_2B_2, *J*=9 Hz, aromatic proton); MS *m/z* 512 (M^+).

Hydrolysis of Permethylate **5**. To a solution of permethylate **5** (186 mg) in a mixture of dioxane (1 ml) and methanol (1 ml), was added 2 M hydrochloric acid (1 ml) and the solution was stirred at 110 °C for 2 h. The reaction mixture was diluted with water, extracted with ether, washed with water and brine, and dried over Na_2SO_4. The solvent was evaporated to give an oily residue, which was chromatographed on silica gel with chloroform to give an oily aglycone (14 mg) which was identical with an authentic *p*-propenylphenol.[6] The aqueous solution was treated with amberlite IR-45 and evaporated to dryness *in vacuo*. The crude product was subjected to column chromatography on silica gel with methanol–chloroform (3:97 v/v) to give a tri-*O*-methyl-D-apiose (25 mg), $[\alpha]_D^{20}$ −5 (*c*, 0.650, MeOH), and a tri-*O*-methyl-D-glucose (27 mg). These methylated sugars were identical with authentic 2,3,3′-tri-*O*-methyl-D-apiose and 2,3,4-tri-*O*-methyl-D-glucose, respectively. An authentic 2,3,3′-tri-*O*-methyl-D-apiose, $[\alpha]_D^{20}$ −1.7 (*c*, 2.3, MeOH), was obtained from apiin which was isolated from parsley, according to the methods in the literature.[3]

Partial Hydrolysis of **2**. 100 mg of **2** was dissolved in water (3 ml) and 1 g of acidic ion exchange resin Amberlite IR-120 was added to it; this mixture was stirred at 65 °C for 1 h. After filtration, the solvent was evaporated to dryness, then the residue (84 mg) was subjected to column chromatography on silica gel with methanol–chloroform (1:9 v/v) and recrystallized from water to give a phenolic glucoside **6** (31 mg), mp 148—149 °C, $[\alpha]_D^{20}$ −61.8 (*c*, 0.275, MeOH), ^1H NMR (acetone-d_6): 3.40 (2H, d, *J*=7 Hz), 5.04 (1H, d, *J*=7 Hz, glucose H-1), 5.10 (1H, bd, *J*=12 Hz), 5.14 (1H, bd, *J*=20 Hz), 5.68—6.24 (1H, m), 7.14, and 7.26 (2H each, A_2B_2, *J*=8 Hz); MS *m/z* (rel int): 296 (M^+, 0.6), 134 ($C_3H_5-C_6H_4-OH$, 100). These data coincided with those of *p*-allylphenyl *β*-D-glucoside in the literature.[7]

The authors are grateful to Professor Hidemasa Imaseki, Nagoya University, for kindly providing authentic samples of furcatin, and to Professor Koichi Koshimizu, Kyoto University, for kindly supplying the IR and ^1H NMR spectra of authentic *p*-allylphenol. They also would like to thank Dr. Shizuo Sako, Kagoshima University, for his aid in the collection and identification of the plants.

References

1) S. Hattori and H. Imaseki, *J. Am. Chem. Soc.*, **81**, 4424 (1959).
2) H. Ohigashi and K. Koshimizu, *Agric. Biol. Chem.*, **40**, 2283 (1976).
3) R. K. Hulyalkar, J. K. N. Jones, and M. B. Perry, *Can. J. Chem.*, **43**, 2085 (1965).
4) H. Herissey, *C. R. Acad. Sci.*, **198**, 256 (1934).
5) R. Higuchi, M. Aritomi, and D. M. X. Donnelly, *Phytochemistry*, **16**, 1007 (1977).
6) An authentic *p*-(1-propenyl)phenol was obtained from methyl *p*-(1-propenyl)phenyl ether (anethole, Wako Prue Chemical Ind.) by alkaline demethylation. R. Stoermer and F. Kahlert, *Ber.*, **34**, 1812 (1901).
7) R. Higuchi and D. M. X. Donnelly, *Phytochemistry*, **16**, 1587 (1977).