Isolation and Absolute Structures of the Neolignan Glycosides with the Enantiometric Aglycones from the Leaves of *Viburnum awabuki* K. KOCH¹⁾

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Received December 15, 1995; accepted January 18, 1996

Two neolignan glycosides, dihydrodehydrodiconiferyl alcohol 4-*O*- β -D-glucopyranosides with the enantiometric aglycones (1 and 2), have been isolated from the leaves of *Viburnum awabuki* K. KOCH. These structures were identified by spectroscopic evidence and the absolute configurations of these compounds were elucidated on the basis of circular dichroism data.

Key words *Viburnum awabuki*; Caprifoliaceae; neolignan glycoside; CD

In the chemical study of *Viburnum awabuki* K. KOCH, a fish poison plant, a number of constituents such as vibsanines,²⁾ coumarin glycosides and triterpenoids³⁾ were isolated. In a previous paper, we reported the isolation of flavonoid glycosides⁴⁾ from the leaves of this plant. As a part of continuing studies on the constituents of the genus *Viburnum* (Caprifoliaceae), we now report the isolation and elucidation of the absolute structures of two dihydrodehydrodiconiferyl alcohol 4-*O*- β -D-glucopyranosides with enantiometric aglycones.

The isolation and purification of the compounds are described in detail in the Experimental section.

Compound **1** was obtained as an amorphous powder, $[\alpha]_D -6.9^\circ$. The ¹H-NMR spectrum of **1** exhibited trimethylene proton signals [δ 1.81 (2H, m), 2.62 (2H, t), 3.56 (2H, t)], two methoxyl group signals [δ 3.83 (3H, s), 3.86 (3H, s)], a methine proton signal [δ 5.56 (1H, d, $J=5.9$ Hz)] and five aromatic proton signals at δ 6.72—7.14. In the ¹³C-NMR spectrum, the presence of a dihydrobenzofuran skeleton and a glucose were suggested. The nuclear Overhauser effect correlation spectroscopy (NOESY) spectrum showed a cross peak between the glucosyl anomeric proton and the H-5 at the *ortho*-position, so that it was apparent that the glucosyl moiety is attached to the C-4 hydroxyl group. From the $J_{H7,H8}$ (5.9 Hz) coupling constant of **1**, it was exhibited that the

configuration of H-7 and H-8 was *trans*.

Absolute configurations were assigned on the basis of circular dichroism (CD) spectroscopic evidence. The CD spectrum of **1** showed the transition at 239 and 221 nm with opposite signs, that is, **1** has a negative Cotton effect at 239 nm and a positive one at 221 nm. Compound **1** shows UV maxima at 277 nm, however, the CD absorption corresponding to this band was very low. Lemiere *et al.* reported that the configurations at C-7 and C-8 of the dihydrobenzofuran skeleton can be clearly distinguished from the 240—220 nm region.⁵⁾ Therefore, the absolute configurations of **1** were determined to be 7*R*,8*S*-configurations.

7*R**,8*S**-dihydrodehydrodiconiferyl alcohol 4-*O*- β -D-glucopyranoside was isolated from *Epimedium diphyllum* by Miyase *et al.*, but its absolute configurations were not elucidated completely.⁶⁾

Compound **2** was obtained as an amorphous powder, $[\alpha]_D -33.4^\circ$. Interestingly, the ¹H- and ¹³C-NMR spectra of **2** were very similar to those of **1**; the structure of **2** was identified to be dihydrodehydrodiconiferyl alcohol 4-*O*- β -D-glucopyranoside by spectroscopic analysis. Accordingly, the aglycone parts of **1** and **2** were deduced to be enantiometric structures, as shown in Chart 1.

In contrast with the CD spectrum of **1**, **2** had a positive Cotton effect at 242 nm and a negative one at 221 nm.

Fig. 1. CD Spectra of Compounds **1** (---) and **2** (—) in H₂O

1 = 3.0×10^{-5} mol/l; **2** = 2.0×10^{-5} mol/l.

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Chart 1

Therefore, the absolute configurations of **2** were determined to be 7*S*,8*R*-configurations.

Compound **2**, which has an enantiomer of **1** as its aglycone moiety, is a new natural compound.

This is the first example of the isolation of dihydrodehydrodiconiferyl alcohol 4-*O*- β -D-glucopyranosides (**1** and **2**) with the enantiometric aglycone, and is the unambiguous determination of the absolute structures of these compounds.

Experimental

Optical rotations were determined with a JASCO DIP-360 digital polarimeter. UV spectra were recorded with a Beckman DU-64 spectrometer. CD spectra were recorded with a JASCO J-700 spectropolarimeter. ^1H - and ^{13}C -NMR spectra were recorded with a JEOL JNM-GSX 400 (400 and 100 MHz, respectively) or 270 (270 and 67.8 MHz, respectively) spectrometer. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane as an internal standard (s, singlet; d, doublet; t, triplet; dd, double doublet; m, multiplet). Column chromatography was carried out on Kieselgel 60 (Merck; 230–400 mesh) and Sephadex LH-20 (Pharmacia Fine Chemicals). Preparative HPLC was carried out on a Tosoh HPLC system (pump, CCPM; detector, UV-8000) using a TSK gel ODS-120A (Tosoh) column.

Extraction and Isolation Fresh leaves of *V. awabuki* (4 kg), collected in October 1993 in Sendai, Japan, were extracted with MeOH at room temp. for 1 month. The MeOH extract was concentrated *in vacuo* and the residue was suspended in water. The water layer was successively extracted with CHCl_3 , Et_2O , AcOEt and *n*-BuOH. The BuOH-soluble part (30 g) was chromatographed on a Sephadex LH-20 column (MeOH– H_2O , 1:1), and then an ODS column. The MeOH– H_2O (1:4) eluate was purified by a silica gel column (CHCl_3 –MeOH– H_2O , 30:10:1), and then subjected to prep. HPLC [ODS-120A 7.8 mm i.d. $\times$ 30 cm, MeOH– H_2O (1:3)] to give **1** (5 mg) and **2** (3 mg).

Compound 1 Amorphous powder. $[\alpha]_{\text{D}}^{20} -6.9^\circ$ ($c=0.4$, MeOH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3344, 1605, 1518. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 226 (3.9), 277 (3.4). FAB-MS m/z : 523 $[\text{M}+\text{H}]^+$. CD nm ($\Delta\epsilon$): 221 (+13.90), 239 (–18.15), 283 (–9.70). ^1H -NMR (CD_3OD , 270 MHz) δ : 1.81 (2H, m, H-8'), 2.62 (2H, t, H-7'), 3.56 (2H, t, H-9'), 3.83 (3H, s, OCH_3 at C-3), 3.86 (3H, s, OCH_3 at C-3'), 5.56 (1H, d, $J=5.9$ Hz, H-7), 6.72 (2H, d, $J=1.9$ Hz, H-2' and H-6'), 6.93 (1H, dd, $J=1.9, 8.5$ Hz, H-6), 7.03 (1H, d, $J=1.9$ Hz, H-2), 7.14 (1H, d, $J=8.5$ Hz, H-5). ^{13}C -NMR (CD_3OD , 67.8 MHz) δ : 32.9 (C-7'), 35.8 (C-8'), 55.6 (C-8), 56.7 and 56.8 ($\text{OCH}_3 \times 2$), 62.2 (C-9'), 62.5 (C-6'), 65.1 (C-9), 71.3 (C-4'), 74.4 (C-2'), 77.8 (C-5'), 78.2 (C-3'), 88.5 (C-7), 102.8 (C-1'), 112.2 (C-2), 114.3 (C-2' or C-6'), 118.0 (C-2' or C-6'), 118.2 (C-5), 119.4 (C-6), 129.6 (C-5'), 137.1 (C-1'), 138.4 (C-1), 145.2 (C-3'), 147.5 (C-4 or C-4'), 147.6 (C-4 or C-4'), 150.9 (C-3).

Compound 2 Amorphous powder. $[\alpha]_{\text{D}}^{20} -33.4^\circ$ ($c=0.7$, MeOH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3344, 1605, 1518. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 227 (4.0), 277 (3.4). FAB-MS m/z : 523 $[\text{M}+\text{H}]^+$. CD nm ($\Delta\epsilon$): 221 (–18.61), 242 (+8.14), 290 (+5.49). ^1H -NMR (CD_3OD , 400 MHz) δ : 1.80 (2H, m, H-8'), 2.62 (2H, t, H-7'), 3.56 (2H, t, H-9'), 3.83 (3H, s, OCH_3 at C-3), 3.86 (3H, s, OCH_3 at C-3'), 5.55 (1H, d, $J=5.9$ Hz, H-7), 6.71 (1H, d, $J=1.8$ Hz, H-2'), 6.73 (1H, d, $J=1.8$ Hz, H-6'), 6.93 (1H, dd, $J=1.8, 8.4$ Hz, H-6), 7.03 (1H, d, $J=1.8$ Hz, H-2), 7.14 (1H, d, $J=8.4$ Hz, H-5). ^{13}C -NMR (CD_3OD , 100 MHz) δ : 32.9 (C-7'), 35.9 (C-8'), 55.7 (C-8), 56.7 and 56.8 ($\text{OCH}_3 \times 2$), 62.3 (C-9'), 62.5 (C-6'), 65.1 (C-9), 71.4 (C-4'), 74.9 (C-2'), 77.9 (C-5'), 78.2 (C-3'), 88.5 (C-7), 102.8 (C-1'), 111.2 (C-2), 114.2 (C-6'), 118.0 (C-5 or C-2'), 118.2 (C-5 or C-2'), 119.4 (C-6), 129.6 (C-5'), 137.1 (C-1'), 138.4 (C-1), 145.3 (C-3'), 147.5 (C-4 or C-4'), 147.7 (C-4 or C-4'), 151.0 (C-3).

Acknowledgments The authors are grateful to Dr. S. Suzuki, Dr. K. Hisamichi and Mr. S. Sato of this college for measurements of the FAB-MS and NMR spectra, respectively.

References and Notes

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