Isolation and Absolute Structures of Enantiomeric 1,2-Bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-Glucosides from the Bark of *Hovenia trichocarpa*

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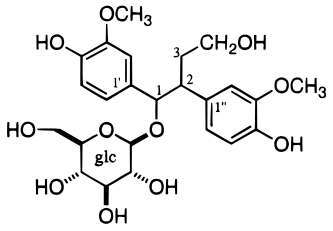
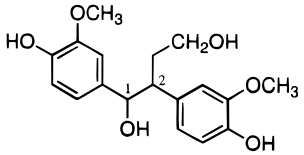
Two 1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-glucosides, hovetrichosides A (**1**) and B (**2**), were isolated from the bark of *Hovenia trichocarpa*. Their structures were established by extensive NMR experiments and chemical methods. Compounds **1** and **2** were (1*R*),(2*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-*β*−D-glucopyranoside and (1*S*),(2*R*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-*β*−D-glucopyranoside, respectively.

Hovenia trichocarpa Chun & Tsiang (Rhamnaceae), a deciduous tree up to 20 m high, is indigenous to the southern part of Japan. The bark of this species is used as a remedy for crapulence and as an underarm deodorant.[1] Recently, we reported the isolation of five new phenolics, named hovetrichosides C−G from the fresh bark of this plant.[2] Further fractionation by Si gel and reversed-phase HPLC gave hovetrichosides A (**1**) and B (**2**), along with other phenolics. We describe here the isolation and structure elucidation of **1** and **2** by various NMR techniques, including COSY, HMQC, HMBC, TOCSY, and ROESY experiments and chemical degradation.



hovetrichoside A (**1**) : 1*R*, 2*S*
hovetrichoside B (**2**) : 1*S*, 2*R*

Compounds **1** and **2** were obtained as pale yellow powders. The common molecular formula, $C_{23}H_{30}O_{11}$ for **1** and **2**, is based on a quasi-molecular ion peak at *m*/*z* 505 $[M + Na]^+$, 521 $[M + K]^+$ in the FABMS, and the number of signals observed in the ^{13}C NMR spectra. The IR absorption maxima at 3395, 1605, and 1520 cm^{-1} and the λ_{max} at 210, 233, and 278 nm in the UV spectra suggested the presence of an aromatic ring. The ^{13}C NMR spectra revealed 17 signals; these were sorted, by DEPT experiments, into MeO × 2, OCH_2 × 1, OCH × 1, CH × 1, =CH × 6, and =C × 6 (Table 1), except for the six signals due to a hexose, indicating that **1** and **2** were 1,2- or 1,3-biphenyl 1,3-propanediol monosaccharides. The ^1H NMR spectrum of **1** exhibited, in the aromatic region, two sets of ABX-type signals at *δ* 7.46 (1H, d, *J* = 2.0 Hz), 7.20 (1H, dd, *J* = 8.0, 2.0 Hz), and 7.16 (1H, d, *J* = 8.0 Hz) and at *δ* 7.23 (1H, d, *J* = 2.0 Hz), 7.09 (1H, d, *J* = 8.0 Hz), and 7.03 (1H, dd, *J* = 8.0, 2.0 Hz) and two methoxy signals at *δ* 3.64 and 3.62, indicating that compound **1** had two guaiacyl groups. ABMX-type signals were observed in the aliphatic region at *δ* 6.05 (d, *J* = 4.5 Hz), 4.75 (dd, *J* = 11.0, 8.0 Hz), 4.20 (dd, *J* = 11.0, 5.5 Hz), and 3.58 (ddd, *J* = 8.0, 5.5, 4.5 Hz). The HMBC experiment revealed long-range coupling from H-1 to C-2, C-3, C-1′, C-2′, C-6′, C-1″, and C-1 of the hexosyl; and from H-2 to C-1, C-3, C-1′, C-1″, 2″ and C-6″. These correlations indicated that **1** and **2** were 1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-saccharides. Enzymatic hydrolysis of **1** and **2** afforded 1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (**3a**) and 1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (**3b**), respectively,[3−8] and D-glucose was confirmed by specific rotation using chiral detection in HPLC analysis.[2] Furthermore, the coupling constant (*J* = 7.5 Hz) observed for the anomeric protons in the ^1H NMR spectra of **1** and **2** indicated the *β*-glucoside linkage for the D-glucose moiety.



compound **3a** : 1*R*, 2*S*
compound **3b** : 1*S*, 2*R*

Compounds **3a**, $[\alpha]^{25}_D$ −40.5° (*c* 1.2, MeOH), and **3b**, $[\alpha]^{25}_D$ + 41.0 (*c* 0.7, MeOH), each revealed a $[M - H]^-$ at *m*/*z* 319 in the negative FABMS. Their spectroscopic properties were the same except for opposite rotary polarizations, establishing that they were enantiomers. The relative stereochemistry of C-1 and C-2 of **3** was determined to be erythro by comparing the NMR spectra with those of erythro and threo isomers.[9] The absolute stereochemistry of C-1 and C-2 was established by the glycosylation shift rule,[10] taking account of threo isomers. The Δ values of +4.2 ppm for C-1 and −2.7 ppm for C-2 in **1** and +7.7 ppm for C-1 and −0.7 ppm for C-2 in **2** established the C-1(*R*), C-2(*S*) in **3a**, the C-1(*S*),

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Table 1. ^{1}H and ^{13}C NMR Data (600 and 150 MHz) for Hovetrichosides A (**1**) and B (**2**), and Compound **3** in Pyridine-d_5

	1		**2**		**3**	
carbon no.	^{13}C	^{1}H, mult	^{13}C	^{1}H, mult	^{13}C	^{1}H, mult
1	78.8	6.05 d (4.5)	82.3	5.98 d (3.5)	74.6	5.74 d (5.0)
2	55.5	3.58 ddd (8.0, 5.5, 4.5)	55.7	3.67 ddd (9.5, 5.5, 3.5)	57.1	3.64 dt (5.0, 6.5)
3	64.0	4.75 dd (11.0, 8.0)	63.7	4.88 dd (10.5, 9.5)	64.5	
		4.20 dd (11.0, 5.5)		4.32 dd (10.5, 5.5)		4.37 dd (10.0, 6.5)
1′	132.9		133.5		137.1	
2′	112.3	7.46 d (2.0)	112.4	7.20 d (2.0)	111.6	7.29 d (2.0)
3′	148.2		148.0		148.2	
4′	147.1		147.0		146.9	
5′	115.8	7.16 (d) (8.0)	115.8	7.09 d (8.0)	115.9	7.16 d (8.0)
6′	120.8	7.20 dd (8.0, 2.0)	120.6	7.12 dd (8.0, 2.0)	120.2	7.20 dd (8.0, 2.0)
1″	131.2		131.2		132.6	
2″	114.6	7.23 d (2.0)	115.5	7.25 d (2.0)	114.8	7.27 d (2.0)
3″	147.9		147.9		148.1	
4″	146.6		146.8		146.7	
5″	115.7	7.09 d (8.0)	115.0	7.08 d (8.0)	115.8	7.16 d (8.0)
6″	123.3	7.03 dd (8.0, 2.0)	123.3	7.14 dd (8.0, 2.0)	123.3	7.20 dd (8.0, 2.0)
MeO 3′	55.7	3.62 s	55.7	3.58 s	55.7	3.62 s
MeO-3″	55.7	3.64 s	55.9	3.65 s	55.8	3.66 s
glc 1	102.7	4.98 d (7.5)	104.7	5.30 d (7.5)		
2	75.3	4.16 dd (8.5, 7.5)	76.4	4.22 m		
3	79.1	4.15 dd (8.5, 8.5)	78.7	4.22 m		
4	72.6	4.12 dd (8.5, 8.5)	71.6	4.24 m		
5	78.1	3.97 ddd (8.5, 5.5, 2.5)	78.5	3.81 m		
6	63.5.	4.65 dd (11.5, 2.5)	62.6	4.63 dd (11.5, 2.5)		
		4.31 dd (11.5, 5.5)		4.24 dd (11.5, 5.5)		

C-2(*R*) in **3b**. Consequently, the structures of **1** (hovetrichoside A) and **2** (hovetrichoside B) were concluded to be (1*R*),(2*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-β-D-glucopyranoside and (1*S*),(2*R*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol 1-*O*-β-D-glucopyranoside, respectively.

1,2-Bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol has been obtained only as a racemate and its relative configuration elucidated (threo or erythro), either as natural products[2,4−7] or synthetic products.[3,8] To the best of our knowledge, **3a** and **3b** are the first naturally occurring optically active compounds of 1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol.

Experimental Section

General Experimental Procedures. Optical rotations were taken on a JASCO DIP-360 polarimeter. IR spectra were recorded on a JASCO FT/IR-5300; NMR spectra, on Varian UNITY 600 and/or JEOL GSX-400 spectrometer in pyridine-d_5 solutions using TMS as internal standard. NMR experiments included ^{1}H−^{1}H COSY, ^{13}C−^{1}H COSY, HMBC, TOCSY, and ROESY. Coupling constants (*J* values) are given in Hertz. The FABMS (Xe gun, 10 kV, triethylene glycol as the matrix) was measured on a JEOL JMS-PX303 mass spectrometer. HPLC separations were performed with a Hitachi HPLC system (L-7100 Pump, L-4000 UV).

Plant Material. Bark of *Hovenia trichocarpa* was collected in April 1995. A voucher specimen (TB 5421) is deposited in the Herbarium of the Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima, Japan.

Extraction and Isolation. Fresh bark (10 kg) of *H. trichocarpa*, collected in Tokushima Prefecture, in April 1995, was extracted with absolute EtOH at room temperature for 6 weeks. The EtOH extract (200 g) was partitioned between H_2O and EtOAc. The H_2O layer was passed through an Amberlite XAD-2 column. After the column was washed with H_2O, the adsorbed materials were eluted with 20% MeOH, 50% MeOH, and 100% MeOH. The 50% MeOH eluate (9 g) was chromatographed on Si gel with CH_2Cl_2−MeOH−EtOAc−H_2O (2:2:4:1, lower layer) to give five fractions (1−5). Fraction 4 (22.5 g) was subjected to HPLC on ODS (Develosil Lop ODS, 70% MeOH) to give five subfractions. Subfractions 2 and 3 were purified by preparative HPLC (YMC, ODS S-5, 3−5% CH_3CN) to afford hovetrichosides A (**1**, 40 mg) and B (**2**, 30 mg).

Hovetrichoside A (1): An amorphous powder; $[\alpha]^{25}_D$ −62.8° (*c* 1.2, MeOH); UV (MeOH) λ_{max} (log ϵ) 210 (4.26), 228 (4.24), 280 (3.87); FT-IR (dry film) ν_{max} 3395 (OH), 1605, 1520 (aromatic) cm^{-1}; NMR, see Table 1; FABMS *m/z* $[M + K]^+$ 521, $[M + Na]^+$ 505.

Hovetrichoside B (2): an amorphous powder; $[\alpha]^{25}_D$ +24.1° (*c* 0.7, MeOH); UV (MeOH) λ_{max} (log ϵ) 208 (4.01), 230 (3.86), 256 (3.45), 261 (3. 39), 280 (3.46); FT-IR (dry film) ν_{max} 3395 (OH), 1605, 1520 (aromatic) cm^{-1}; NMR, see Table 1; FABMS *m/z* $[M + K]^+$ 521, $[M + Na]^+$ 505.

Enzymatic Hydrolysis of Hovetrichoside A (1). A solution of **1** (20 mg) in EtOH (0.2 mL) and 0.01M NaH_2PO_4 buffer (pH4.0, 1.8 mL) was incubated with crude cellulase (20 mg, Sigma) for one week at 37 °C. The reaction mixture was passed through a column of Amberlite XAD-2, and washed with H_2O, and then eluted with MeOH. From the H_2O eluate, D-(+)-glucose was detected by using RI detection (Waters 410) and chiral detection (Shodex OR-1) in HPLC (Shodex RSpak NH_2P-50 4E, 95%CH_3CN containing 1%H_3PO_4, 1 mL/min, 47 °C) by comparison with an authentic sugar (each 10 mmol D-glc and L-glc). The sugar portion gave the following peak: D-(+)-glc 25.4 min. The crude hydrolysate (12 mg) obtained from the MeOH was chromatographed on a Si gel column with $CHCl_3$−MeOH−H_2O (25:2:0.1) to give **3a** (8 mg) as an amorphous powder: $[\alpha]^{25}_D$ −40.5° (*c* 0.7, MeOH); NMR data,

see Table 1; FABMS *m*/*z* $[M - H]^-$ 319; EIMS *m*/*z* $[M - 18]^+$ 302 (40), 284 (35), 272 (90), 150 (75), 135 (55), 84 (100).

Enzymatic Hydrolysis of Hovetrichoside B (2). A solution of **2** (20 mg) was carried out in the same way as described for **1**. The MeOH gave **3b** (8 mg) as an amorphous powder: $[\alpha]^{25}_D$ +41.0° (*c* 0.7, MeOH); NMR data, see Table 1; FABMS *m*/*z* $[M - H]^-$ 319. From the H_2O water eluate, D-glucose was detected.

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References and Notes

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(9) Miyase, T. *School of Pharmaceutical Sciences, University of Shizuoka*, personal communication to the NMR data of compound **3**, 1998. NMR data (pyridine-d_5), erythro isomer: δ 74.9 (C-1), 64.7 (C-2), 57.0 (C-2), 5.73 (1H, d, J = 5.5 Hz), threo isomer: δ 78.0 (C-1), 66.0 (C-2), 56.3 (C-2), 5.61 (1H, d, J = 8.0 Hz).
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