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Absolute configuration of resveratrol oligomer glucosides isolated from the leaves of *Upuna borneensis*

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ABSTRACT

A comprehensive investigation of the chemical constituents of the leaves of *Upuna borneensis* (Dipterocarpaceae) was performed. Three new glucosides of resveratrol oligomers having a pentameric aglycone [upunoside E (**1**)] and dimeric aglycones [upunosides F (**3**) and G (**4**)], as well as 14 resveratrol derivatives (**2**, **5**–**17**), were isolated. The absolute configurations of the new compounds were elucidated by spectroscopic analysis, including two-dimensional NMR and CD spectra.

1. Introduction

The leaves of evergreen trees belonging to the Dipterocarpaceae family are important sources of the scaffolds of stilbene oligomers (Dai et al., 1998; Ito et al., 2005d, 2010, 2013). The woody plant *Upuna borneensis* Sym. is a monotypic genus distributed in Malaysia and Indonesia. We have focused on the chemical constituents in the woody parts of this plant, resulting in the discovery of various new phenolic compounds, specifically resveratrol derivatives and acetophenones (Ali et al., 2004; Ito et al., 2007, 2009a, 2005a, 2005b; Ito et al., 2005c, 2004). Our preliminary study showed that the leaves also contain high quantities of stilbene derivatives (Ito et al., 2005d). In the present study, a comprehensive investigation of the chemical constituents of the leaves of *U. borneensis* was performed, resulting in the isolation and characterization of a new *O*-glucoside of resveratrol pentamer [upunoside E (**1**)] and two new *O*-glucosides of resveratrol dimer [upunosides F (**3**) and G (**4**)], along with 14 known resveratrol derivatives (**2**, **5**-**17**). The structures of the new compounds (**1**, **3**, and **4**) were elucidated by 2D NMR techniques including double-quantum-filtered correlation spectroscopy (DQF-COSY), heteronuclear multiple-quantum coherence spectroscopy (HMQC), heteronuclear multiple-bond correlation spectroscopy (HMBC), and NOESY as well as high-resolution (HR) ESI–MS analysis and CD spectrometry.

2. Materials and methods

2.1. General experimental procedure

The following instruments were used: a JASCO P-1020 polarimeter for optical rotations; a JASCO J-820 spectrometer (in MeOH solution) for UV and CD spectra; a JEOL JNM ECA-500 spectrometer for ^{1}H and ^{13}C NMR spectroscopy (chemical shift values in ^{1}H NMR spectra were presented as δ values with TMS as the internal standard); and an Shimadzu LCMS-IT-TOF mass spectrometer for ESIMS. Moreover, a Shimadzu HPLC system (Shimadzu Corporation, Japan) was used in this study. The system consisted of an SCL-10AVP system controller, two LC-6AD pumps, a DGU-20A3 on-line degasser, a CTO-10AVP column oven, a SIL-10AXL autosampler, and an SPD-10A UV–vis detector. The flow-rate of the mobile phase in HPLC was 5 ml/min, and detection was performed at 280 nm. The chromatographic data were collected and processed using Shimadzu CLASS-VP software (version 6.14, Shimadzu Corporation, Japan). The following adsorbents were used for purification: Merck Kieselgel 60 F_{254} (0.25 mm) for analytical TLC; Merck Kieselgel 60, Fuji Silysia Chemical Chromatorex, and Waters Sep-Pak C_{18} cartridges for column chromatography; a Capcell Pak C_{18} column (UG120, 250 × 10 mm i.d., SHISEIDO, Japan) for preparative HPLC.

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Table 1
NMR data of upunoside E (**1**).

No.	δ_H	δ_C	HMBC	NOESY
1a		131.2		
2a(6a)	7.20 (d, 8.0)	130.3	4a, 7a	7a, 8a, 14a
3a(5a)	6.79 (d, 8.0)	116.2	1a, 4a	
4a		158.3		
7a	5.75 (d, 11.7)	89.8	2a(6a), 8a, 9a	2a(6a), 14a
8a	4.29 (br d, 11.7)	50.2	1a, 7a, 9a, 10b	2a(6a), 2b(6b)
9a		141.7		
10a		124.2		
11a		155.6		
12a	6.25 (d, 2.1)	101.5	10a, 11a, 13a, 14a	
13a		156.6		
14a	6.18 (br d, 2.1)	105.5	10a, 12a, 13a	2a(6a), 7a
1b		133.1		
2b(6b)	6.97 (d, 8.0)	130.5	4b, 7b	7a, 7b, 8c
3b(5b)	6.71 (d, 8.0)	115.6		
4b		155.7		
7b	5.10 (d, 3.2)	37.1	10a, 1b, 8b, 9b, 1c	2b(6b)
8b	3.17 (br d, 11.6, 3.2)	52.4	9b	7c, 14c
9b		141.7		
10b		115.6		
11b		152.3		
12b		112.6		
13b		156.9		
14b				
1c		130.5		
2c(6c)	6.44 (d, 8.0)	129.0	7c	7c, 8c
3c(5c)	6.42 (d, 8.0)	115.7		
4c				
7c	3.95 (t,11.6)	58.9	8b, 9b, 8c	8b, 2c(6c), 14c
8c	4.43 (d, 11.6)	50.4	13b, 9c	2b(6b), 2c(6c)
9c		141.5		
10c		121.6		
11c		162.8		
12c	6.43 (d, 2.0)	109.4	10c, 11c, 13c	
13c		160.3		
14c	6.64 (br d, 2.0)	108.0	8c, 10c, 13c,	8b, 7c
1d		133.7		
2d(6d)	7.20 (d, 8.6)	127.5	4d, 7d	7d, 8d
3d(5d)	6.93 (d, 8.6)	116.3	7d	
4d		158.1		
7d	5.42 (d, 3.4)	94.2	11c, 2d(6d), 9d	2d(6d), 10d(14d)
8d	4.44 (d, 3.4)	56.6	11c, 1d, 9d, 10d(14d)	2d(6d), 10d(14d)
9d		146.9		
10d	6.02 (br d, 1.8)	106.7	8d	7d, 8d
11d		159.7		
12d	6.22 (t,1.8)	102.4	10d(14d), 11d(13d)	
13d		131.2		
14d		130.3		7d, 8d
1e		136.7		
2e(6e)	7.27 (d, 8.6)	130.0	7e	7e, 8e
3e(5e)	6.71 (d, 8.6)	115.5		
4e		158.1		
7e	4.47 (d, 5.7)	44.0	11b, 13b, 1e, 2e(6e)	2e(6e), 14e
$8e_A$	2.98 (dd, 5.7, 12.5)	39.1	7e	14e, Glc-1
$8e_B$	3.62 (d,12.5)		7e, 10e, 14e	
9e		144.9		
10e	6.44 (br d, 1.8)	97.2	8e, 11e, 12e,	
11e		159.5	11e, 13e, 14e	
12e	6.53 (br s)	102.1		
13e		158.0	8e, 10e, 12e	
14e	6.28 (br s)	110.9	10e, 12e	7e
Glc-1	4.87 (d, 7.5)	101.8		8e
Glc-2	3.55 (m)	74.6		
Glc-3	3.44 (m)	77.3		
Glc-4	3.37 (m)	71.3		
Glc-5	3.55 (m)	77.9		
Glc-6	3.75 (br d, 10.9)	62.3		
	3.30 (m)			
OH-13b	4.91 (s)			

Values are in ppm (δ_H and δ_C). Measured in acetone-d_6 at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR).
All protons and carbons were assigned by DQF-COSY, HMQC and HMBC spectra.

2.2. Plant material

Leaves of *U. borneensis* Sym. were collected at Bogor Botanical Garden, Bogor, Indonesia in May 2000. Voucher specimens DP-029 have been deposited at Gifu Pharmaceutical University, Gifu, Japan.

2.3. Extraction and isolation

The extraction procedures are described in our previous paper (Ito et al., 2005d, 2012). The acetone extract (120 g) of leaves of *U. borneensis* (580 g) was subjected to RP column chromatography (CC) on DMS eluted with a mixture of MeOH-H_2O, MeOH, acetone, and $CHCl_3$, to give 53 fractions (^{A}Fr. 1–^{A}Fr. 53). Compound **7** (28 mg) were purified from a part of the combined fractions of ^{A}Fr. 15–^{A}Fr. 17 (Fr. E) [25%MeOH–30%MeOH]] by PTLC [EtOAc-$CHCl_3$-MeOH-H_2O (15:8:4:1)]. Purification of the combined fractions of ^{A}Fr. 23–^{A}Fr. 30 (Fr. G) [30%MeOH–35%MeOH]] by Sephadex LH-20 CC (MeOH), RP CC through Sep-Pak cartridges (H_2O-MeOH gradient system), PTLC [EtOAc-$CHCl_3$-MeOH-H_2O (15:8:4:1 and 80:40:11:2)], and reversed-phase HPLC (H_2O-MeOH) achieved the isolation of **4** (40 mg), **10** (9 mg), **13** (30 mg), **15** (43 mg), and **17** (17 mg). The combined fractions of ^{A}Fr. 33–^{A}Fr. 41 (Fr. J) [35% MeOH−50%MeOH]] were further purified by the same procedure for Fr. G to give **1** (9 mg), **3** (24 mg), **5** (44 mg), **6** (23 mg), **8** (3 mg), **11** (7 mg), **12** (12 mg), **14** (12 mg), and **16** (3 mg).

The MeOH extract (72 g) was subjected to CC on ODS eluted with a mixture (MeOH−H_2O gradient system) to give 42 fractions (^{M}Fr. 1–^{M}Fr. 42). Compounds **2** (5 mg) and **9** (9 mg) were purified from ^{M}Fr. 18 [40% MeOH] by Sephadex LH-20 CC (MeOH), Si gel CC (EtOAc-$CHCl_3$-MeOH-H_2O gradient system), and RP CC through Sep-Pak cartridges (H_2O–MeOH gradient system).

2.3.1. Upunoside E (*1*)

A pale-yellow solid; α_D^{25}+2° (c 0.10, MeOH); UV λ_{max} (MeOH): 226 (3.95), 282 (3.56); CD (*c* 7.7 μM, MeOH) nm (Δe) 203 (−48.0), 216 (+48.3), 236 (−29.6); ^{1}H and ^{13}C NMR spectroscopic data in acetone-d_6, Table 1; ESIMS, *m/z* 1297.4041 [M+H]$^+$ (calculated for $C_{76}H_{65}O_{20}$, 1297.4069).

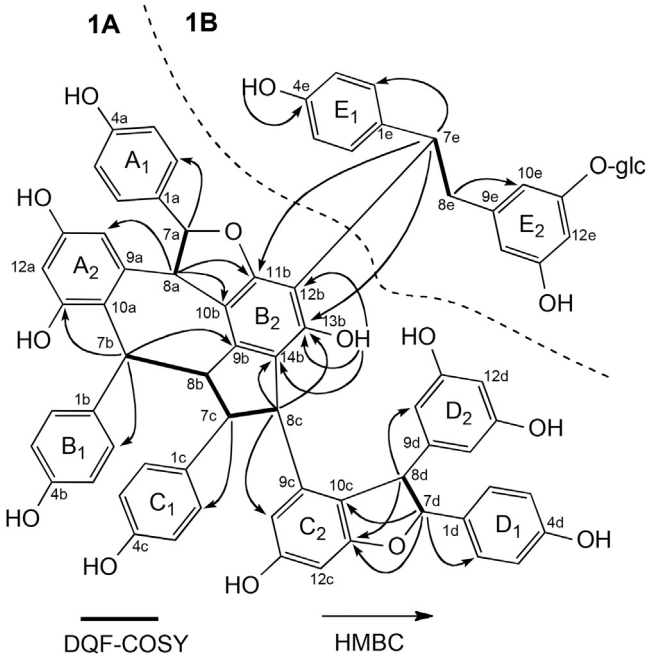

Fig. 1. Selected 2D NMR correlations for **1**.