Resveratrol Tetramers with a C_6–C_3 or a C_1 Unit from *Upuna borneensis*

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Investigation of the chemical constituents in the stem of *Upuna borneensis* (Dipterocarpaceae) resulted in the isolation of three new resveratrol derivatives, upunaphenols L (1), M (2) (resveratrol tetramers with a C_6–C_3 unit) and N (3) (resveratrol tetramer with a C_1 unit). The structures have the same partial structure as vaticanol B (4). Upunaphenols L and M are new complex polyphenol compounds, lignostilbene. Their structures were determined by spectroscopic analysis including two dimensional NMR. Upunaphenol M was found to be an artifact generated by silica gel catalyzed methanolysis of 1.

Key words *Upuna borneensis*; Dipterocarpaceae; resveratrol oligomer; upunaphenol; silica-gel catalyzed methanolysis

In our previous papers of the chemical constituents of *Upuna borneensis* (Dipterocarpaceae), the structure of new resveratrol derivatives (upunaphenols A—K,[1—4] upunosides A—D[5]) were described. Further search for components with biological activities in the stem of *U. borneensis* resulted in the isolation of three new resveratrol derivatives. In the present paper, the isolation and characterization of three new compounds, upunaphenols L (**1**)—N (**3**), is described.

Results and Discussion

Upunaphenols L (**1**) ($[\alpha]_D^{25}$ −13°), M (**2**) ($[\alpha]_D^{25}$ +8°), and N (**3**) ($[\alpha]_D^{25}$ −31°) were purified from an acetone-soluble part of stem of *U. borneensis* by column chromatography over silica gel, Sephadex LH-20, ODS, and PTLC (preparative TLC). All compounds showed positive reactions to the Gibbs reagent.

Upunaphenol L (**1**) was obtained as a yellow solid. In the high resolution (HR)-FAB-MS, an $[M-H]^-$ ion peak was observed at *m*/*z* 1051.2979 suggesting the molecular formula of $C_{65}H_{48}O_{14}$. An absorption band (1744 cm^{-1}) in the IR spectrum and a signal (δ_C 167.7) in the ^{13}C-NMR spectrum showed the presence of an ester carbonyl group (C-9e) in the molecule. The ^{1}H- and ^{13}C-NMR spectral data together with ^{1}H–^{1}H shift correlation spectroscopy (COSY), ^{13}C–^{1}H COSY and ^{1}H detected heteronuclear multiple bond connectivity (HMBC) spectra (Table 1) showed the presence of *ortho*-coupled aromatic protons assignable to five 4-hydroxylphenyl groups (rings A_1—E_1), two sets of *meta*-coupled aromatic protons on a 1,2,3,5-tetrasubstituted benzene ring (rings A_2 and C_2) and a 3,5-dihydroxyphenyl group (D_2). The NMR spectral data also disclosed the presence of two sets of aliphatic signals characteristic for 2,3-diaryldihydrobenzofuran moieties (H-7a and H-8a; H-7d and H-8d),[1—5] a sequence of four aliphatic methine protons successively coupled in this order (H-7b/H-8b/H-7c/H-8c) and a methine–methylene system (H-7e/H-8e$_A$/H-8e$_B$). The ^{1}H-NMR spectrum measured in DMSO-d_6 exhibited signals for 10 phenolic hydroxyl groups (δ_H 8.98—9.58) which disappeared upon addition of D_2O. Considering the molecular formula, the remaining three oxygens could be allotted to ether linkages. In the HMBC spectrum (Fig. 1), significant ^3J correlations were observed between H-7a/C-2a(6a), H-14a/C-8a, H-7b/C-2b(6b), H-7c/C-2c(6c), H-8c/C-14c, H-7d/C-2d(6d), H-10d(14d)/C-8d and H-7e/C-2e(6e), indicating that rings A_1, A_2, B_1, C_1, C_2, D_1, D_2, and E_1 are attached at C-7a, C-8a, C-7b, C-7c, C-8c, C-7d, C-8d and C-7e, respectively. Further correlations observed between H-7b/C-9a and H-8d/C-11c supported the connections between C-7b/C-10a and C-8d/C-10c, respectively. After complete assignment of all the quaternary carbons in rings A_1—E_1, A_2, C_2 and D_2, the remaining six quaternary aromatic carbons (C-9b—C-14b) in the ^{13}C-NMR spectrum (δ_C 142.4, 120.2, 155.1, 107.7, 149.2, 124.1) were assigned to those of a 1,3-dioxygenated benzene ring (B_2). Similar patterns were also observed in vaticanols I and J,[6] and upunoside A,[5] where one of the aromatic rings was fully substituted and based on a 1,3-dioxygenated pattern. Two oxygenated carbon signals (C-11b and C-13b) correlated with H-7e, which indicated that C-7e was linked to C-12b. The other C–C linkages attached to ring B_2 (C-8a—C-10b, C-8b—C-9b, C-8c—C-14b) were substantiated by the correlations of H-8a/C-11b, H-7b/C-9b and H-8c/C-13b, re-

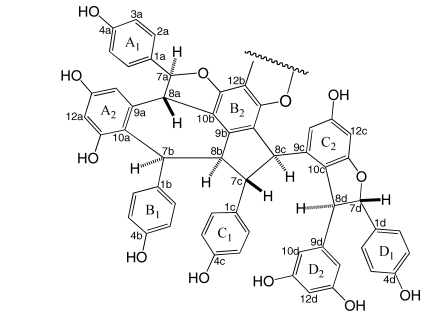

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Table 1. ^{1}H- and ^{13}C-NMR Spectral Data of **1**—**3**

Position	**1**		**2**		**3**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1a		130.4		131.3		129.6
2a, 6a	7.18 (d, 8.6)	130	7.30 (d, 8.6)	130.0	7.28 (d, 8.6)	130.4
3a, 5a	6.74 (d, 8.6)	116.3	6.79 (d, 8.6)	116.1	6.82 (d, 8.6)	116.4
4a (OH)		158.1		158.5	8.60 (br s)	159.0
7a	5.93 (d, 11.9)	91.2	5.81 (d, 11.8)	90.0	6.06 (d, 11.7)	92.8
8a	4.48 (br d, 11.9)	49.3	4.40 (br d, 11.8)	49.4	4.49 (br d, 11.7)	48.2
9a		140.8		141.5		140.7
10a		124.6		124.4		124.3
11a (OH)		155.7		156.4	8.31 (br s)	155.9
12a	6.31 (d, 2.2)	101.8	6.27 (d, 2.0)	101.7	6.33 (d, 2.2)	102.2
13a (OH)		156.8[a]		156.6	8.18 (br s)	157.0
14a	6.14 (d, 2.2)	105.9	6.16 (br d, 2.0)	105.8	6.16 (d, 2.2)	105.7
1b		133.1[b]		133.3		133.0
2b, 6b	7.13 (d, 8.6)	130.4	7.06 (d, 8.6)	130.6	7.16 (d, 8.6)	130.5
3b, 5b	6.66 (d, 8.6)	115.5	6.65 (d, 8.6)	115.5	6.75 (d, 8.6)	115.8
4b (OH)		155.9		155.7		133.0
7b	5.16 (d, 3.7)	37	5.15 (d, 4.0)	37.0	5.26 (d, 3.5)	36.9
8b	3.21 (br d, 11.4)	53	3.15 (br d, 11.3)	52.8	3.16 (br d, 11.2)	54.0
9b		142.4		140.2		153.7
10b		120.2		116.9		115.9[c]
11b		155.1		156.7		161.9
12b		107.7		113.4		107.2
13b (OH)		149.2	5.15 (s)	151.5	11.26 (s)	158.6
14b		124.1		121.3		122.3
1c		130.9		130.5		130.8
2c (6c)	6.53 (d, 8.6)	129.5	6.40 (d, 8.6)	129.1	6.45 (d, 8.6)	129.3
3c (5c)	6.61 (d, 8.6)	116.1	6.45 (d, 8.6)	115.9	6.53 (d, 8.6)	116.0
4c (OH)		156.5		156.3	7.97 (br s)	156.6
7c	4.18 (dd, 11.4, 10.6)	58.6	4.02 (t, 11.3)	58.1	4.15 (t, 11.2)	56.8
8c	4.55 (d, 10.6)	49.4	4.47 (d, 11.3)	50.0	4.55 (d, 11.2)	48.8
9c		140.9		140.7		140.3
10c		123		121.3		123.9
11c		161.8		162.7		161.8
12c	6.15 (d, 2.0)	96.1	6.39 (d, 2.0)	97.0	6.25 (d, 2.0)	95.9
13c (OH)		158.7		160.9	8.21 (br s)	159.3
14c	6.53 (d, 2.0)	107.1	6.54 (d, 2.0)	107.5	6.48 (d, 2.0)	106.8
1d		132.6		133.7		134.8
2d, 6d	7.31 (d, 8.6)	129.7	7.20 (d, 8.6)	127.5	7.22 (d, 8.6)	128.1
3d, 5d	6.76 (d, 8.6)	115.7	6.91 (d, 8.6)	116.3	6.85 (d, 8.6)	115.9[c]
4d (OH)		157.1		158.2	8.41 (br s)	158.2
7d	5.33 (d, 9.3)	95.1	5.45 (d, 3.7)	94.2	5.38 (d, 4.7)	94.5
8d	4.67 (d, 9.3)	58.4	4.43 (d, 3.7)	57.1	4.62 (d, 4.7)	57.6
9d		146.1		146.9		147.8
10d, 14d	6.07 (d, 2.2)	110.8[d]	6.03 (d, 2.2)	107.0	6.12 (d, 2.2)	107.5
11d, 13d (OH)		159.1		159.9	8.02 (br s)	159.8
12d	6.26 (t, 2.2)	102.2	6.26 (t, 2.0)	102.5	6.30 (t, 2.2)	102.2
1e		133.1[b]		135.9		
2e (6e)	7.02 (d, 8.6)	128.7	7.22 (d, 8.6)	129.7		
3e (5e)	6.72 (d, 8.6)	116	6.66 (d, 8.6)	115.7		
4e		156.8[a]		155.9		
7e	4.46 (dd, 6.6, 2.2)	35	4.72 (dd, 8.9, 7.6)	37.5		
$8e_A$	3.13 (dd, 15.7, 6.6)	37.2	3.18 (dd, 15.5, 8.9)	39.2		
$8e_B$	2.97 (dd, 15.7, 2.2)		3.04 (dd, 15.5, 7.6)			
9e		167.7		173.2		
OMe			3.51	51.3		
CHO					10.00 (s)	192.6

Measured in acetone-d_6 at 300 MHz (^{1}H-NMR) and 75 MHz (^{13}C-NMR). All protons were assigned by ^{1}H–^{1}H, ^{1}H–^{1}H long-range, ^{13}C–^{1}H COSY, COLOC and HMBC spectrum. *a*—*c*) Overlapping. *d*) Broad signal.

spectively. The C–C bond of C-8e/C-9e was further deduced by correlations of H-7e/C-9e and H-8e/C-9e. An additional cross peak observed between H-7d/C-11c supported the presence of an ether linkage (C-7d/O/C-11c), which formed a dihydrobenzofuran ring (C-7d/C-8d/C-10c/C-11c/O). Another ether linkage (C-7a/O/C-11b) and the ester linkage (C-13b/O/C-9e, IR: 1744 cm^{-1}) were deduced after considering the carbon chemical shifts and the molecular formula. The planar structure of upunaphenol L, which included two dihydrobenzofuran rings and a six-membered lactone ring, was concluded to be **1**. The other correlations in the HMBC spectrum, as summarized in the experimental section, were in ac-

cordance with this proposed planar structure. The structure can be regarded as a complex product composed of a resveratrol tetramer unit [resveratrols A—D (resveratrol A: ring A_1–C-7a–C-8a–ring A_2)] and a phenylpropan (ring E_1–C-7e–C-9e). The planar structure of the tetrameric unit is identical to four known diastereomeric resveratrol tetramers of vaticanol B (**4**),[1,7,8] isovaticanol B,[1,8] and viniferols B and C.[9] The stereostructure of **1** was determined by analysis of the NOESY spectrum (Fig. 2). The *trans* relationship of H-7a/H-8a on the dihydrobenzofuran ring was confirmed by the distinctive NOEs between H-7a/H-14a, H-8a/H-2a(6a) and H-2(6a)/H-14a. The large coupling constant values of H-7a and H-8a (J=11.9 Hz) also supported the stereo relationships.[7—9] The *trans* relationship of H-7d/H-8d on the other dihydrobenzofuran ring was confirmed by the same manner. In addition, the syn orientation of ring B_1, H-8a, H-7c and ring C_2 was supported by the NOEs between H-2b(6b)/H-8a, H-2b(6b)/H-7c and H-2b(6b)/H-14c. The *axial* orientations of H-8b, H-7c and H-8c were unambiguously evidenced by the J_{vic} values and confirmed by the distinct NOE observed for H-8b/H-8c. The relative configuration of the tetrameric unit (resveratrols A—D) was concluded to be the same as that of **4**. The remaining stereogenetic carbon (C-7e) was elucidated to be relative-*S* configuration by the NOE for H-2e(6e)/H-2d(6d).

Upunaphenol M (**2**) was obtained as a pale yellow amorphous powder. HR-FAB-MS (*m*/*z* 1083.3242 $[M-H]^-$) showed a molecular formula of $C_{66}H_{52}O_{15}$. The ^{1}H- and ^{13}C-NMR spectral data (Table 1) indicated the presence of four resveratrol units (resveratrols A—D) and a phenylpropan (ring E_1–C-7e–C-9e). The structure was determined by the same manners as **1**. Analysis of the ^{1}H- and ^{13}C-NMR, ^{1}H–^{1}H COSY, ^{13}C–^{1}H COSY, HMBC and NOESY data confirmed that **2** also had a vaticanol B unit. The spectra were closely similar to those of **1**, except for the signals of an additional phenolic hydroxyl (OH-13b) and a methoxyl group. In the HMBC spectrum, the correlations between H-OMe/C-9e, H-7e/C-9e and H-7e/C-2e(6e) (Fig. 3) were observed, which revealed the presence of a 3-(4-hydroxyphenyl)-propionic acid methyl ester unit. Two carbon signals (C-11b and C-13b) were correlated with H-7e, which indicated that C-7e was linked to C-12b. Correlations of OH (δ_H 5.15) with the aromatic carbons at C-12b, C-13b and C-14b revealed that C-13c of the ring B_2 is substituted with the hydroxyl group. Therefore, the structure of upunaphenol M including relative stereochemistry can be presented as **2**.

In the ^{1}H-NMR spectrum, the signal of OH-13b in **2** was observed at δ_H 5.15, while the same proton in **4** was at 7.61.[7] Similar behaviors based on hydroxyl groups have also been observed for upunoside A (δ_H 5.02),[5] vaticanol J (δ_H 5.30),[6] and pauciflorol D (δ_H 4.70),[10] all of which bear the same partial structure composed of ring B_2–C-7e–ring E_1. The upper field shift of OH-13b can be explained by the anisotropy caused by the ring E_1. Although, compounds **1**, **2**

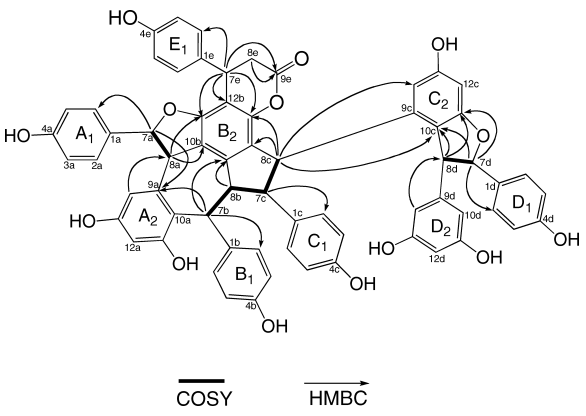

Fig. 1. Selected Correlations Observed in 2D NMR of **1**
Other HMBC correlations: see Experimental.

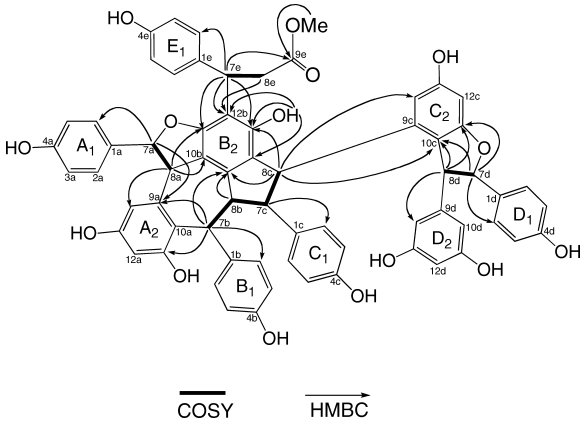

Fig. 3. Selected Correlations Observed in 2D NMR of **2**
Other HMBC correlations: see Experimental.

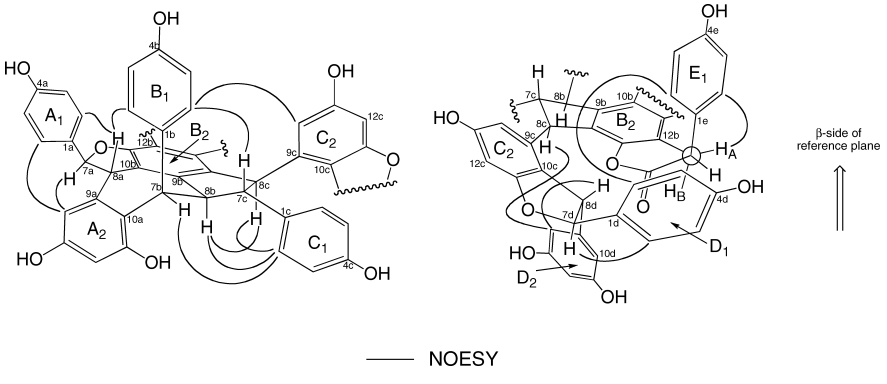

Fig. 2. Relative Structure and NOEs Observed for the Partial Structures [Resveratrols A—C: Left Figure; Resveratrols B—D and C_6–C_3 Unit (Ring E_1–C-7–C-9): Right Figure] of **1**
Other NOESY correlations: see Experimental.

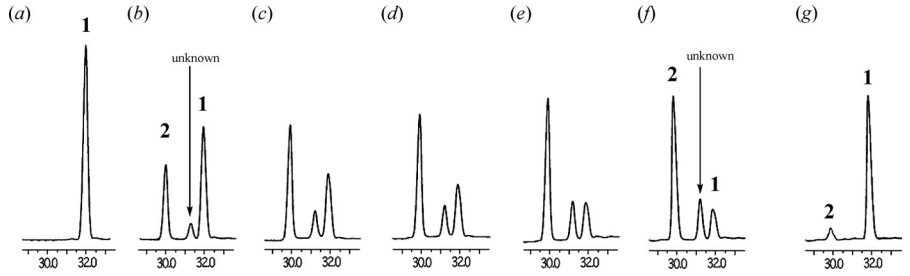

Fig. 4. HPLC of Reaction Mixtures of **1**

(a)—(f) Silica gel, MeOH, reflux; (a) 0 h, (b) 1 h, (c) 2 h, (d) 3 h, (e) 4 h, (f) 6 h and (g): 3% H_2SO_4, MeOH, reflux, 6 h.

and **4** have the same partial structure in resveratrols A—D, the *J*-values between H-7d/H-8d were quite different (**1**: 9.3 Hz, **2**: 3.7 Hz, **4**: 4.7 Hz[7]). The lactone ring in **1** would cause a conformational change in the dihydrobenzofuran ring. Compound **2** is probably generated *via* **1** during the isolation, which is supported by the following fact. The HPLC of the extract and a crude fraction did not show the presence of **2**. When **1** was refluxed in MeOH under existence of silica gel, **1** was converted to **2** through time dependent [Fig. 4, (a)—(f)], which was analysed by HPLC. On the other hand, reflux of **1** in MeOH under acidic condition slightly gave **2** (Fig. 4, (g)). These fact strongly indicated that **2** was generated by silica gel catalyzed methanolysis of **1** during isolation and is an artifact.

Upunaphenol N (**3**) was obtained as a yellow amorphous powder. The composition was deduced to be $C_{57}H_{42}O_{13}$ by the $[M-H]^-$ ion peaks observed at *m/z* 933.2560 in the HR-FAB-MS. The patterns of NMR spectral data (Table 1) were closely similar to those of **4**, except for an appearance of an aldehyde group (IR 1613 cm^{-1}; ^{13}C-NMR δ_C 192.6) instead of aromatic proton on C-12b. In the correlation spectroscopy involving long-range coupling (COLOC) spectrum (see Experimental), the aromatic carbon (C-12b) was correlated with the aldehyde proton (δ_H 10.00), which indicated that the aldehyde group was located at C-12b. The structure of upunaphenol N was determined to be **3**.

The structural differences among **1**—**4** were attributable to the substituents on the ring B_1. The co-occurrence of **1**—**4**, which involves the common vaticanol B unit, adds a biogenetic relationship among them. Upunaphenol L (**1**) is a first instance of lignostilbenoids in Dipterocarpaceaeous plants, which would be formed by a fusion of the ring B_2 and a phenylpropan unit. The skeleton bears a dihydroneoflavone moiety.

In addition to these three compounds (**1**—**3**), astragalin-6″-*trans*-*p*-coumalate was also isolated. The structure was identified by the spectral comparison with those of literature data.[11] Flavonoids have rarely been isolated from Dipterocarpaceaeous plants. This is the first report of flavonoids from *Upuna borneensis*.

Experimental

The following instruments were used: optical rotations, JASCO P-1020 polarimeter; UV spectra, Shimadzu UV-2200 spectrophotometer (in MeOH solution); IR spectra: JASCO FT-IR-8000 spectrophotometer (KBr micro plate; in cm^{-1}); ^{1}H- and ^{13}C-NMR spectra, JEOL JNM LA-300 and EX-400 (chemical shift values are presented as δ values with TMS as internal standard); EI-MS and FAB-MS, JEOL JMS-DX-300 instrument.

The following adsorbents were used for purification: analytical TLC, Merck Kieselgel 60 F_{254} (0.25 mm); preparative TLC, Merck Kieselgel 60 F_{254} (0.5 mm); column chromatography, Merck Kieselgel 60, Pharmacia Fine Chemicals AB Sephadex LH-20 and Fuji Silysia Chemical Chromatorex.

Upuna borneensis Sym. was cultivated in Bogor Botanical Garden, Bogor, Indonesia, and its stems were collected in May 2000 and identified by one of co-authors (D.D.). A voucher specimen (number DP-012) has been deposited in Gifu Pharmaceutical University.

Extraction and Isolation of Compounds (**1**—**3**, astragalin-6″-*trans*-*p*-coumalate) The extraction procedure is the same as that on our previous reports.[1—5] Fr. 6 ($CHCl_3$–MeOH, 9 : 1) was further subject to Sephadex LH-20 CC (MeOH) to give seven fractions (Fr. 6a–Fr. 6g). Astragalin-6″-*trans*-*p*-coumalate (4 mg) was purified from the fraction Fr. 6e after PTLC ($CHCl_3$–MeOH–H_2O, 14 : 6 : 1). Fr. 10 ($CHCl_3$–MeOH, 6 : 1) was fractionated into six parts (Fr. 10a–Fr. 10f) by Sephadex LH-20 CC (MeOH). Subfraction of Fr. 10e gave **1** (31 mg) and **2** (25 mg) after purification by repeated Sephadex LH-20 CC (MeOH) and PTLC (EtOAc–$CHCl_3$–MeOH–H_2O, 15 : 8 : 4 : 1). Compound **3** (330 mg) were purified from fraction Fr. 10f after CC over silica gel (EtOAc–$CHCl_3$–MeOH–H_2O, 15 : 8 : 4 : 1).

Compound **1** (Upunaphenol L): A yellow amorphous powder; $[\alpha]_D$ −13° (*c*=0.1, MeOH); UV (MeOH) λ_{max} (log ε): 214 (4.51), 225sh (4.49), 284 (3.76) nm; IR ν_{max} (KBr) 3387, 1744, 1608, 1512, 1448, 1338, 1240, 1171 cm^{-1}; negative ion FAB-MS *m/z*: 1051 $[M-H]^-$; negative ion HR-FAB-MS *m/z*: 1051.2979 $[M-H]^-$ (Calcd for $C_{65}H_{47}O_{14}$: 1051.2965); ^{1}H- and ^{13}C-NMR spectral data [^{1}H (300 MHz), ^{13}C (75 MHz), acetone-d_6], See Table 1; ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) δ: 7.04 (2H, d, *J*=8.6 Hz, H-2a(6a)), 6.68 (2H, d, *J*=8.6 Hz, H-3a(5a)), 5.85 (1H, d, *J*=11.6 z, H-7a), 4.24 (1H, d, *J*=11.6 Hz, H-8a), 6.14 (1H, d, *J*=2.0 Hz, H-12a), 5.88 (1H, br s, H-14a), 6.94 (2H, d, *J*=8.6 Hz, H-2b(6b)), 6.62 (2H, d, *J*=8.6 Hz, H-3b(5b)), 4.91 (1H, d, *J*=4.0 Hz, H-7b), 2.80 (1H, br d, *J*=11.2 Hz, H-8b), 6.28 (2H, d, *J*=8.6 Hz, H-2c(6c)), 6.52 (2H, d, *J*=8.6 Hz, H-3c(5c)), 3.95 (1H, dd, *J*=11.2, 10.8 Hz, H-7c), 4.42 (1H, d, *J*=10.8 Hz, H-8c), 6.03 (1H, d, *J*=2.0 Hz, H-12c), 6.25 (1H, br d, *J*=2.0 Hz, H-14c), 7.18 (2H, d, *J*=8.6 Hz, H-2d(6d)), 6.64 (2H, d, *J*=8.6 Hz, H-3d(5d)), 5.28 (1H, d, *J*=9.6 Hz, H-7d), 4.49 (1H, d, *J*=9.6 Hz, H-8d), 5.98 (2H, br s, H-10d(14d)), 6.10 (1H, t, *J*=2.0 Hz, H-12d), 6.87 (2H, d, *J*=8.6 Hz, H-2e(6e)), 6.66 (2H, d, *J*=8.6 Hz, H-3e(5e)), 4.30 (1H, br d, *J*=5.6 Hz, H-7e), 2.95 (1H, br d, *J*=14.4 Hz, H-8e), 3.18 (1H, dd, *J*=14.4, 5.6 Hz, H-8e), 8.98 (2H br s, phenolic OH), 9.04, 9.08, 9.11, 9.13, 9.19, 9.34, 9.38, 9.58 (1H each, s, phenolic OH×8); HMBC correlations, see Fig. 1 (selected) and H-2a(6a)/C-4a, C-7a; H-3a(5a)/C-1a, C-4a; H-7a/C-1a, C-8a, C-9a; H-8a/C-7a; H-12a/C-10a, C-11a, C-13a, C-14a; H-14a/C-10a, C-12a, C-13a; H-2b(6b)/C-4b, C-7b ; H-3b(5b)/C-1b, C-4b; H-7b/C-10a, C-1b, C-7c; H-2c/C-4c, C-7c; H-3c(5c)/C-1c, C-4c; H-7c/C-1c, C-8b, C-8c, C-9c; H-8c/C-9c; H-12c/C-10c, C-11c, C-13c, C-14c; H-14c/C-10c, C-12c, C-13c; H-2d(6d)/C-4d, C-7d; H-3d(5d)/C-1d, C-4d; H-7d/C-1d, C-8d, C-9d; H-8d/C-1d, C-7d, C-9d, C-9c; H-10d(14d)/C-11d(13d), C-12d; H-12d/C-11d(13d); H-2e(6e)/C-4e, C-7e; H-3e(5e)/C-1e, C-4e; H-7e/C-1e, H-8e$_A$/C-12b, C-1e, C-7e; H-8e$_B$/C-12b, C-1e, C-7e; NOESY correlations: see Fig. 2 (selected) and H-2a(6a)/H-7a; H-2b(6b)/H-7b; H-2c(6c)/H-7c; H-2d(6d)/H-7d; H-2e(6e)/H-7e.

Compound **2** (Upunaphenol M): A pale yellow amorphous powder; $[\alpha]_D$ +8° (*c*=0.1, MeOH); UV (MeOH) λ_{max} (log ε): 208 (4.52), 225sh (4.43), 283 (3.99) nm; IR ν_{max} (KBr) 3395, 1608, 1516, 1448, 1368, 1242, 1170 cm^{-1}; negative ion FAB-MS *m/z*: 1083 $[M-H]^-$; negative ion HR-FAB-MS *m/z*: 1083.3242 $[M-H]^-$ (Calcd for $C_{66}H_{51}O_{15}$: 1083.3227); ^{1}H- and ^{13}C-NMR spectral data [^{1}H (300 MHz), ^{13}C (75 MHz), acetone-d_6], see Table 1; HMBC correlations: See Fig. 3 (selected) and H-2a(6a)/C-4a, C-7a; H-3a(5a)/C-1a, C-4a; H-7a/C-1a, C-8a, C-9a; H-8a/C-7a; H-12a/C-10a, C-11a, C-13a, C-14a; H-14a/C-10a, C-12a, C-13a; H-2b(6b)/C-4b, C-7b; H-

3b(5b)/C-1b, C-4b; H-7b/C-10a, C-1b, C-7c; H-2c/C-4c, C-7c; H-3c(5c)/C-1c, C-4c; H-7c/C-1c, C-8b, C-8c, C-9c; H-8c/C-9c; H-12c/C-10c, C-11c, C-13c, C-14c; H-14c/C-10c, C-12c, C-13c; H-2d(6d)/C-4d, C-7d; H-3d(5d)/C-1d, C-4d; H-7d/C-1d, C-8d, C-9d; H-8d/C-1d, C-7d, C-9d, C-9c; H-10d(14d)/C-11d(13d), C-12d; H-12d/C-11d(13d); H-2e(6e)/C-4e, C-7e; H-3e(5e)/C-1e, C-4e; H-7e/C-1e, H-8e$_A$/C-1e, C-9e; H-8e$_B$/C-1e, C-9e; NOESY correlations: H-2a(6a)/H-7a, H-8a; H-7a/H-2a(6a); H-8a/H-2a(6a), H-2b(6b); H-2b(6b)/H-8a, H-7b, H-7c; H-7b/H-2b(6b), H-2c(6c); H-8b/H-2c(6c); H-2c(6c)/H-7b, H-8b, H-8c; H-7c/H-2b(6b), H-14c; H-8c/H-2c(6c); H-14c/H-7c; H-2d(6d)/H-7d, H-8d; H-7d/H-2d(6d), H-10d(14d); H-8d/H-2d(6d), H-10d(14d); H-10d(14d)/H-7d, H-8d; H-2e(6e)/OH-13b, H-7e, H-8e$_A$; H-7e/OH-13b, H-2e(6e); H-8e$_A$/H-2e(6e); OH-13b/H-2e(6e), H-7e.

Compound **3** (Upunaphenol N): A yellow amorphous powder; $[\alpha]_D$ −31° (c=0.1, MeOH); UV (MeOH) λ_{max} (log ε): 212 (4.49), 225sh (4.43), 284 (3.94) nm; IR ν_{max} (KBr) 3400, 1613, 1513, 1442, 138, 1240, 1172 cm^{-1}; negative ion FAB-MS m/z: 933 $[M-H]^-$; negative ion HR-FAB-MS m/z: 933.2560 $[M-H]^-$ (Calcd for $C_{57}H_{41}O_{13}$: 933.2547); ^{1}H- and ^{13}C-NMR spectral data [^{1}H (300 MHz), ^{13}C (75 MHz), acetone-d_6], see Table 1; COLOC correlations: C-1a/H-3a(5a), H-7a, H-8a; C-2a(6a)/H-7a; C-3a(5a)/OH-4a; C-4a/H-2a(6a), OH-4a; C-7a/H-2a(6a), H-8a; C-8a/H-7a, H-14a; C-9a/H-7b; C-10a/H-8a, OH-11a; C-11a/H-12a, H-7b, OH-11a; C-12a/H-14a, OH-11a, OH-13a; C-13a/H-12a, H-14a, OH-13a; C-14a/H-8a, H-12a, OH-13a; C-1b/H-3b(5b), H-7b, H-8b; C-2b(6b)/H-7b; C-3b(5b)/OH-4b; C-4b/H-2b(6b), OH-4b; C-7b/H-2b(6b); C-9b/H-7b, H-8b; C-10b/H-8a; C-12b/CHO-12b, OH-13b; C-13b/OH-13b; C-14b/OH-13b, H-8c; C-1c/H-3c(5c), H-7c; C-2c(6c)/H-7c; C-3c(5c)/OH-4c; C-4c/H-2c(6c), OH-4c; C-7c/H-2c(6c); C-8c/H-14c; C-9c/H-7c; C-10c/H-12c, H-14c, H-8d; C-11c/H-12c, H-7d, H-8d; C-12c/H-14c, OH-13c; C-13c/H-12c, H-4c, OH-13c; C-14c/H-8c, H-12c, OH-13c; C-1d/H-3d(5d), H-7d, H-8d; C-2d(6d)/H-7d; C-3d(5d)/OH-4d; C-4d/H-2d(6d), OH-4d; C-7d/H-2d(6d); C-9d/H-7d; C-10d(14d)/H-8d, H-12d, OH-11d(13d); C-11d(13d)/H-12d, H-14d, OH-11d(13d); C-12d/OH-11d(13d); NOESY correlations: H-2a(6a)/H-7a, H-8a; H-7a/H-2a(6a); H-8a/H-2a(6a), H-2b(6b); H-2b(6b)/H-8a, H-7b, H-7c; H-7b/H-2b(6b), H-2c(6c); H-8b/H-2c(6c); H-2c(6c)/H-7b, H-8b, H-8c; H-7c/H-2b(6b), H-14c; H-8c/H-2c(6c); H-14c/H-7c; H-2d(6d)/H-7d, H-8d; H-7d/H-2d(6d), H-10d(14d); H-8d/H-2d(6d), H-10d(14d); H-10d(14d)/H-7d, H-8d.

Methanolysis of **1**: Upunaphenol L (**1**, 1.0 mg) was dissolved in MeOH (10 ml), silica gel (0.1 g: Merck Kieselgel 60 (70—230 mesh)) was added and stirred under reflux for 6 h. The reaction solution was collected at 0 h and after 1 h, 2 h, 3 h, 4 h and 6 h. Each reactant was immediately filtered to apply to HPLC analysis. To a solution of upunaphenol L (0.1 mg) in MeOH (1.0 ml), 6% H_2SO_4 (1.0 ml) was added and refluxed for 6 h. The reaction solution was partitioned and extracted with ethyl acetate (30 ml), and the ethyl acetate layer was washed with water and brine, dried over anhydrous sodium sulfate. The solvent was removed and the crude product was dissolved in MeOH (1.0 ml) to afford HPLC analysis.

HPLC analysis: The system was consisted of a LC-10AD pump, a SIL-10AD auto injector, a SCL-10A system controller, and a SPD-10AV UV–Vis absorbance detector, equipped by CLASS-VP software. The separation was performed on a Capcell Pak C_{18} UG120 S-5 (5 μm, 250×4.6 mm; SHISEIDO, Japan) at 40 °C. The mobile phase consisted of MeOH–1% AcOH; 20 to 50% MeOH in 30 min, maintain 50% to 40 min. The flow-rate of the mobile phase was 1 ml/min and detection was carried out at 280 nm. Retention times of **1**—**4** were as follows, **1**: t_R 31.9 min; **2**: t_R 29.9 min; **3**: t_R 32.6 min; **4**: t_R 23.8 min.

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