Novel Norsesquiterpenoids from the Roots of *Phyllanthus emblica*

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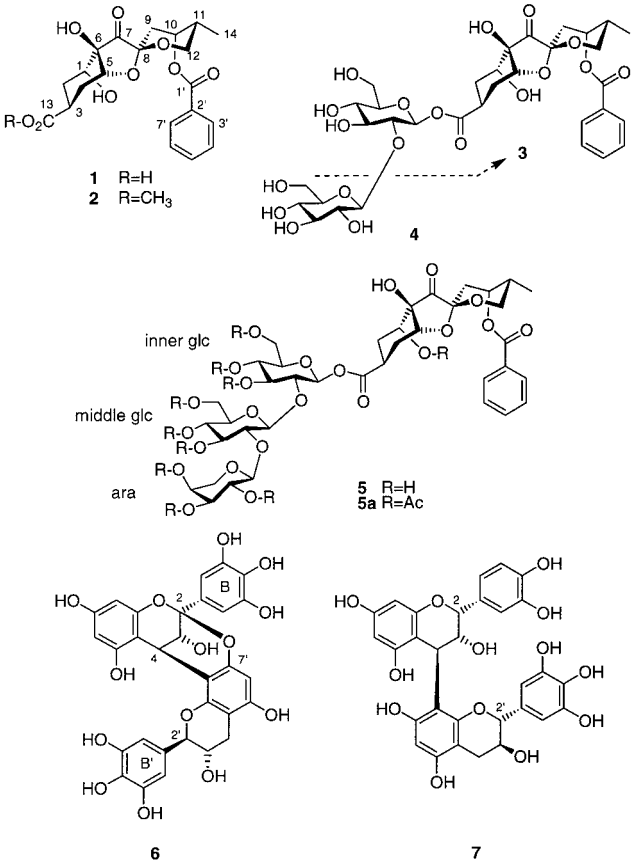
Three ester glycosides, named phyllaemblicins A (**3**), B (**4**), and C (**5**), and a methyl ester (**2**), of a highly oxygenated norbisabolane, phyllaemblic acid (**1**), were isolated from the roots of *Phyllanthus emblica*, along with 15 tannins and related compounds. The structures of **2**−**5** were established by spectral and chemical methods.

Phyllanthus emblica L. (Euphorbiaceae), a shrub or tree growing in subtropical and tropical areas of the People's Republic of China, India, Indonesia, and the Malay Peninsula, has been used widely for its antiinflammatory and antipyretic effects in many local traditional medicinal systems, such as Chinese herbal medicine, Tibetan medicine, and Ayurvedic medicine. The minorities living in the Southwest of China use the roots of *P. emblica* for the treatment of eczema, and in Nepal it is used as an astringent and hematostatic agent.[1] In a previous communication,[2] we reported the structure elucidation including the absolute stereochemistry of a novel highly oxygenated norbisabolane, phyllaemblic acid (**1**), from the roots of this plant. Further investigation has led to the isolation of its methyl ester (**2**) and three novel ester glycosides, phyllaemblicins A (**3**), B (**4**), and C (**5**), along with 15 tannins and related compounds. This paper deals with a full account of the isolation and structural elucidation of **2**−**5**.

Results and Discussion

A 60% aqueous acetone extract of the air-dried roots of *P. emblica* was partitioned between EtOAc and water, and then the organic phase was subjected successively to chromatography over Sephadex LH-20, MCI gel CH20P, Chromatorex ODS, and silica gel to afford compounds **1**−**5** and 15 substances of known structure. By comparison of the physical and spectral data with those of authentic samples, the known compounds were identified as gallic acid, pyrogallol, protocatechuic acid, corilagin,[3] 1,2,3,6-tetra-*O*-galloyl-*β*-D-glucose,[4] 1,2,3,4,6-penta-*O*-galloyl-*β*-D-glucose,[5] (±)-gallocatechin,[6] (−)-epigallocatechin,[7] (+)-catechin,[7] (−)-epicatechin,[7] (−)-epigallocatechin 3-*O*-gallate,[7] (−)-epicatechin 3-*O*-gallate,[7] and epicatechin-(4*β*→8)-epigallocatechin 3-*O*-gallate,[8] respectively. Compounds **6** and **7** were characterized as epigallocatechin-(2*β*→7,4*β*→8)-gallocatechin **(**prodelphinidin A-1) and epicatechin-(4*β*→8)-gallocatechin by negative-ion FABMS and ^{1}H NMR comparison, in turn, with proanthocyanidin A-1[9] and procyanidin B-1.[10] The structure of **7** was also confirmed by thiolysis (mercaptoethanol-HCl), yielding gallocatechin and epicatechin-4-(2-hydroxy)ethylthio ether.[11] The spectroscopic data have been assigned for the first time for compounds **6** and **7**.



The structure of compound **1** was characterized previously as a novel norbisabolane-type terpenoid by spectroscopic and chemical means, and its absolute stereochemistry was determined by applying the modified Mosher's method to an opportune degradation product from our previous work.[2]

Compound **2** was obtained as a white amorphous powder. Comparison of the ^{1}H and ^{13}C NMR spectral data with those of **1** enabled **2** to be assigned as a methyl ester of **1**, and it was confirmed by the treatment of **1** with CH_2N_2, yielding **2**. Hence, **2** was characterized as a methyl ester of phyllaemblic acid.

Compound **3** was obtained as a white amorphous powder. Its molecular formula was assigned as $C_{27}H_{34}O_{14}$ on the basis of the NMR data, the positive-ion FABMS (*m*/*z* 583, $[M + H]^+$), and elemental analysis. The ^{1}H and ^{13}C NMR spectral data of **3** were closely related to those of **1**, except

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for an upfield shift of C-13 (δ 176.2) and the appearance of signals due to a β-D-glucopyranose moiety. Chemical shifts of the anomeric proton [δ_H 5.46 (d, J = 7.5 Hz)] and carbon (δ 95.64) signals indicated that the glucose moiety was attached to the C-13 carboxyl group of **1** through an ester linkage. This was supported by methanolysis with 2% NaOMe yielding **2** and acidic hydrolysis affording glucose and **1**. On the basis of the above results, the structure of **3** was determined as an ester glucoside of **1** and named phyllaemblicin A.

Compound **4** showed the $[M + H]^+$ ion peak at m/z 745 in the FABMS, which was 162 mass units larger than that of **3**. This difference corresponded to the mass of an additional hexopyranose moiety. The ^{1}H and ^{13}C NMR spectra of **4** resembled those of **3**, which exhibited signals due to two hexose moieties together with a set of signals almost superimposable on those of **1**. The sugar moieties were both determined to be glucose by acidic hydrolysis with 0.5 N H_2SO_4, and the configurations of the anomeric positions were assigned as β on the basis of the J values of their anomeric protons (δ 5.59, d, J = 8.0 Hz and δ 4.18, d, J = 8.5 Hz). The HMBC spectrum of **4** showed long-range correlations of the anomeric proton of the inner glucose (δ 5.59) with C-13 (δ 175.8) and the anomeric proton of the terminal glucose (δ 4.18) with C-2 of the inner glucose (δ 83.1), which indicated that the additional glucose moiety was attached to the C-2 position of the glucose moiety of **3** in structure **4**. Accordingly, the structure of **4** was established and named phyllaemblicin B.

The ^{1}H and ^{13}C NMR spectra of compound **5** were closely related to those of **4** except for the appearance of a set of additional sugar signals, indicating that **5** is also a glycoside of **1**. The FABMS (m/z 877, $[M + H]^+$) and elemental analysis enabled the molecular formula $C_{33}H_{44}O_{19}$ to be assigned to **5**. The presence of three sugar residues in **5** was indicated by the appearance of three anomeric proton signals at δ 5.59 (d, J = 8.5 Hz), 4.14 (d, J = 8.0 Hz), and 4.47 (d, J = 7.0 Hz) in the ^{1}H NMR spectrum. Taking the molecular weight into account, the sugar moieties were concluded to be two hexoses and a pentose unit. Acidic hydrolysis of **5** with 0.5 N H_2SO_4 afforded D-glucose ($[\alpha]_D$ +16.3°) and L-arabinose ($[\alpha]_D$ +22.3°). The coupling constants of the anomeric protons of the two glucose moieties indicated their anomeric positions to be in the β configuration, and coupling constants ($J_{1,2}$ = 7.0 Hz, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ < 1 Hz, $J_{4,5}$ = 3.0 and <1 Hz) of the L-arabinose moiety suggested it to be in the α-pyranose form. Connectivities of the sugar moieties were revealed by the HMBC correlations of C-13 with H-1 of the inner glucose, C-2 of the inner glucose with H-1 of the middle glucose, and C-2 of the middle glucose with H-1 of the arabinose, which suggested strongly that the additional arabinose moiety was attached to the C-2 position of the terminal glucose of **4** in structure **5**. This was further confirmed by complete assignments of the sugar proton signals observed in the ^{1}H NMR spectrum of the peracetate **5a**, in which neither of the C-2 methine protons of the glucose units (δ 3.85 and 3.56) showed any acylation shift. On the basis of the above results, the structure of **5** was determined and named phyllaemblicin C.

Although several norbisabolenes with a skeleton representative of the loss of one of the terminal dimethyl carbons are so far known,[16,17] compounds **1**−**5** with a highly oxygenated aglycon are the first norbisabolanes biosynthesized by oxidative removal of the central methyl carbon.[16]

Several bisabolane glycosides, namely, phyllanthoside and the phyllanthostatins,[12,13] isolated from *Phyllanthus brasiliensis*, have been found to inhibit strongly the growth of the murine P-388 lymphocytic leukemia cell line. However, compounds **1** and **3**, with a similar norbisabolane skeleton, showed only weak activity for inhibition of protein kinases[18−20] and no activity on human cancer cell line panel screening.[21,22]

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. ^{1}H and ^{13}C NMR spectra were recorded in CD_3OD with Varian Unity plus 500 and Varian Gemini 300 spectrometers operating at 500 and 300 MHz for ^{1}H and 125 and 100 for ^{13}C, respectively. Coupling constants are expressed in hertz, and chemical shifts are given on a δ (ppm) scale with tetramethylsilane as the internal standard. MS spectra were recorded on a JEOL JMS DX-303 spectrometer, and glycerol was used as a matrix for FABMS measurement. Column chromatography was performed with Kieselgel 60 (70−230 mesh, Merck), MCI-gel CHP 20P (75−150 μm, Mitsubishi Chemical Co.), Sephadex LH-20 (25−100 μm, Pharmacia Fine Chemical Co. Ltd.), and Chromatorex ODS (100−200 mesh, Fuji Silysia Chemical Ltd.). TLC was performed on precoated Kieselgel 60 F_{254} plates (0.2 mm thick, Merck), and spots were detected by ultraviolet (UV) illumination and by spraying with 10% sulfuric acid reagent.

Plant Material. The roots of *Phyllanthus emblica* L. were collected at Wenshan, Yunnan, People's Republic of China. A voucher specimen is deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried roots (8.0 kg) were extracted with 60% aqueous acetone four times at room temperature to give an extract (450 g), which was partitioned between EtOAc (1 L) and H_2O (1 L) four times. After concentration *in vacuo*, the EtOAc layer (46.7 g) was chromatographed on Sephadex LH-20 (60%-100% MeOH then 60% acetone) to afford five fractions (fractions 1−5). Fraction 1 (7.76 g) was separated successively by passage over MCI gel CHP 20P (H_2O−MeOH, 1:0−0:1), Chromatorex ODS (10−70% MeOH), and Si gel ($CHCl_3$−MeOH−H_2O, 9:1:0.1−6:4:1) to afford compounds **2** (518 mg), **3** (190 mg), **4** (430 mg), and **5** (133 mg). Fraction 2 (8.66 g) was chromatographed over Chromatorex ODS (40−100% MeOH), MCI gel CHP 20P (0−30% MeOH), and silica gel ($CHCl_3$−MeOH−H_2O, 9:1:0.1−8:2:0.2) to give **1** (3.4 g), gallic acid (226 mg), and pyrogallol (472 mg). Fractions 3 (6.0 g) and 4 (8.31 g) were chromatographed repeatedly on MCI gel CHP 20P (10−80% MeOH), Sephadex LH-20 (EtOH and 60% MeOH), and Chromatorex ODS (5−50% MeOH) to afford protocatechuic acid (396 mg), corilagin (35 mg), 1,2,3,6-tetra-*O*-galloyl-β-D-glucose (68 mg), 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (102 mg), (±)-gallocatechin (122 mg), and (−)-epigallocatechin (89 mg) from fraction 3, and (+)-catechin (19 mg), (−)-epicatechin (116 mg), (−)-epigallocatechin 3-*O*-gallate (35 mg), (−)-epicatechin 3-*O*-gallate (105 mg), and **6** (64 mg) from fraction 4, respectively. Fraction 5 (14.59 g) was chromatographed over MCI gel CHP 20P (10−90% MeOH) and Chromatorex ODS (10−65% MeOH) to give epicatechin-(4β→8)-epigallocatechin 3-*O*-gallate (456 mg) and **7** (58 mg).

Methyl ester of phyllaemblic acid (2): white amorphous powder; $[\alpha]^{25}_D$ +19.3° (*c* 0.85, MeOH); UV (MeOH) λ_{max} (log ϵ) 272 (3.00), 279 (2.93) nm; IR (KBr) ν_{max} 3406, 2954, 1777, 1718, 1603, 1450, 1277, 1114, 1006 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 8.14 (2H, dd, J = 8.0, 1.5 Hz, H-3′, 7′), 7.61 (1H, tt, J = 1.5, 8.0 Hz, H-5′), 7.48 (2H, br t, J = 8.0 Hz, H-4′, 6′), 5.30 (1H, q, J = 3.0 Hz, H-10), 4.25 (1H, br d, J = 1.8 Hz, H-5), 4.03 (1H, t, J = 11.4 Hz, H-12a), 3.89 (1H, br s, H-1), 3.61 (3H, s, OMe), 3.58 (1H, dd, J = 11.4, 4.2 Hz, H-12b), 2.79 (1H, tt, J = 12.9, 3.0 Hz, H-3) 2.34 (1H, dd, J = 14.7, 3.3 Hz, H-9a), 2.23 (1H, br d, J = 14.4 Hz, H-4a), 2.18 (1H, m, H-11), 1.95 (1H, dd, J = 14.7, 3.3 Hz, H-9b), 1.86 (1H, m, H-2a), 1.82 (1H,

m, H-4b), 1.69 (1H, dt, J = 12.9, 2.4 Hz, H-2b), 0.91 (3H, d, J = 6.9 Hz, H-14); ^{13}C NMR (CD_3OD, 75 MHz) δ 213.8 (C-7), 177.7 (C-13), 167.9 (C-1′), 134.0 (C-5′), 132.1 (C-2′), 130.8 (C-3′, 7′), 129.4 (C-4′, 6′), 100.5 (C-8), 76.3 (C-5), 75.6 (C-6), 71.4 (C-1), 71.2 (C-10), 63.5 (C-12), 52.1 (OMe), 34.2 (C-11), 33.0 (C-2), 32.5 (C-9), 31.8 (C-3), 29.1 (C-4), 13.1 (C-14); FABMS m/z 435 $[M + H]^+$.

Methylation of 1. A solution of **1** (15 mg) in MeOH (2 mL) was treated with CH_2N_2/Et_2O at room temperature. After concentration, the mixture was purified by Si gel column chromatography ($CHCl_3$−MeOH−H_2O, 80:20:2) to afford **2** (8 mg).

Phyllaemblicin A (3): white amorphous powder; $[\alpha]^{25}_D$ +27.9° (c 0.27, MeOH); UV (MeOH) λ_{max} (log ϵ) 273 (2.99), 279 (2.91) nm; IR (KBr) ν_{max} 3292, 2930, 1778, 1720, 1603, 1452, 1286, 1124, 1012 cm^{-1}; ^{1}H NMR (CD_3OD, 500 MHz) δ aglycon 8.13 (2H, d, J = 7.5 Hz, H-3′, 7′), 7.63 (1H, br t, J = 7.5 Hz, H-5′), 7.54 (2H, br t, J = 7.5 Hz, H-4′, 6′), 5.32 (1H, br d, J = 3.5 Hz, H-10), 4.28 (1H, br s, H-5), 4.01 (1H, t, J = 11.5 Hz, H-12a), 3.91 (1H, br s, H-1), 3.57 (1H, dd, J = 11.5, 4.5 Hz, H-12b), 2.95 (1H, t, J = 13.0 Hz, H-3), 2.31 (1H, br d, J = 15.0 Hz, H-4a), 2.27 (1H, dd, J = 15.0, 3.5 Hz, H-9a), 2.18 (1H, m, H-11), 1.99 (1H, dd, J = 15.0, 3.5 Hz, H-9b), 1.93 (1H, br d, J = 13.0 Hz, H-2a), 1.90 (1H, dt, J = 15.0, 4.0 Hz, H-4b), 1.78 (1H, dt, J = 13.0, 2.0 Hz, H-2b), 0.90 (3H, d, J = 7.0 Hz, H-14), glucose: 5.46 (1H, d, J = 8.0 Hz, glc H-1), 3.89 (1H, br d, J = 12.0 Hz, glc H-6a), 3.73 (1H, dd, J = 12.0, 3.5 Hz, glc H-6b), 3.39 (1H, m, glc H-5), 3.31 (2H, m, glc H-3, 4), 3.25 (1H, t, J = 8.0 Hz, glc H-2); ^{13}C NMR (CD_3OD, 125 MHz) δ 213.8 (C-7), 176.2 (C-13), 168.0 (C-1′), 134.4 (C-5′), 132.0 (C-2′), 130.7 (C-3′, 7′), 129.7 (C-4′, 6′), 100.5 (C-8), 76.2 (C-5), 75.5 (C-6), 71.2 (C-1), 71.1 (C-10), 63.4 (C-12), 34.3 (C-11), 32.8 (C-2), 32.6 (C-9), 32.3 (C-3), 29.0 (C-4), 13.1 (C-14); glucose, 95.6 (glc C-1) 78.8 (glc C-5), 78.1 (glc C-3), 74.0 (glc C-2), 71.0 (glc C-4), 62.4 (glc C-6); FABMS m/z 605 $[M + Na]^+$ (22), 583 $[M + H]^+$ (8), 421 $[M - glc]^+$ (63), 299 (52), 105 (100); *anal*. C 53.60%, H 6.08%, calcd for $C_{27}H_{34}O_{14}$·5/4 H_2O, C 53.62%, H 5.93%.

Acidic Hydrolysis of 3. A solution of **3** (1 mg) in 0.5 N H_2SO_4 (0.5 mL) was heated at 80 °C for 1 h. The mixture was neutralized with Amberlite IRA-400 (OH^- form) resin and concentrated to dryness. TLC analysis indicated the presence of compound **1** and glucose [$CHCl_3$−MeOH−H_2O, 7:3:0.5, for glucose (R_f 0.1), and 9:1:0.1 for **1** (R_f 0.5)].

Methanolysis of 3. A solution of **3** (6 mg) in 2% NaOMe in MeOH (1 mL) was left standing at room temperature for 30 min. After neutralization with Amberlite IR-120B (H^+ form) resin, the solution was concentrated to dryness and applied to a Si gel column to afford **2** (2 mg).

Phyllaemblicin B (4): yellowish amorphous powder; $[\alpha]^{25}_D$ +10.4° (c 0.58, MeOH); UV (MeOH) λ_{max} (log ϵ) 272 (2.99), 279 (2.91) nm; IR (KBr) ν_{max} 3205, 2933, 1778, 1718, 1604, 1452, 1294, 1124, 1012 cm^{-1}; ^{1}H NMR (CD_3OD, 500 MHz) δ aglycon: 8.16 (2H, dd, J = 7.5, 1.5 Hz, H-3′, 7′), 7.66 (1H, br t, J = 7.5 Hz, H-5′), 7.57 (2H, br t, J = 7.5 Hz, H-4′, 6′), 5.36 (1H, q, J = 3.0 Hz, H-10), 4.29 (1H, br s, H-5), 4.03 (1H, t, J = 11.0 Hz, H-12a), 3.93 (1H, br s, H-1), 3.58 (1H, br d, J = 11.0 Hz, H-12b), 2.94 (1H, tt, J = 13.5, 2.5 Hz, H-3), 2.36 (1H, br d, J = 13.5 Hz, H-4a), 2.28 (1H, dd, J = 15.0, 3.0 Hz, H-9a), 2.18 (1H, m, H-11), 2.01 (1H, dd, J = 15.0, 3.0 Hz, H-9b), 2.04 (1H, br d, J = 13.5 Hz, H-2a), 1.90 (1H, dt, J = 13.5, 4.0 Hz, H-4b), 1.77 (1H, dt, J = 13.5, 2.5 Hz, H-2b), 0.89 (3H, d, J = 7.0 Hz, H-14); inner glucose, 5.59 (1H, d, J = 8.0 Hz, glc H-1), 4.08 (1H, dd, J = 9.0, 8.0, glc H-2), 3.89 (1H, dd, J = 12.0, 2.5 Hz, glc H-6a), 3.75 (1H, dd, J = 12.0, 5.0 Hz, glc H-6b), 3.62 (1H, t, J = 9.0 Hz, glc H-3), 3.46 (1H, dd, J = 9.5, 9.0 Hz, glc H-4), 3.39 (1H, m, glc H-5), terminal glucose: 4.18 (1H, d, J = 8.0 Hz, glc H-1), 3.62 (1H, dd, J = 12.0, 2.5 Hz, glc H-6a), 3.56 (1H, dd, J = 12.0, 4.5 Hz, glc H-6b), 3.25 (1H, dd, J = 9.5, 9.0 Hz, glc H-4), 3.23 (1H, dd, J = 9.5, 9.0 Hz, glc H-4), 3.11 (1H, dd, J = 9.0, 8.0, glc H-2), 2.76 (1H, m, glc H-5); ^{13}C NMR (CD_3OD, 125 MHz) δ 213.7 (C-7), 175.8 (C-13), 167.8 (C-1′), 134.4 (C-5′), 132.1 (C-2′), 130.8 (C-3′, 7′), 129.9 (C-4′, 6′), 100.5 (C-8), 76.3 (C-5), 75.4 (C-6), 71.5 (C-1), 70.9 (C-10), 63.4 (C-12), 34.3 (C-11), 32.7 (C-9), 32.2 (C-2, 3), 29.3 (C-4), 13.1 (C-14); inner glucose, 93.7 (glc C-1) 83.1 (glc C-2), 78.9 (glc C-5), 77.8 (glc C-3), 70.8 (glc C-4), 62.3 (glc C-6); terminal glucose, 105.9 (glc C-1), 77.7 (glc C-3), 77.6 (glc C-5), 75.9 (glc C-2), 70.7 (glc C-4), 62.0 (glc C-6); FABMS m/z 767 $[M + Na]^+$ (18), 745 $[M + H]^+$ (31), 583 (29), 421 (28), 299 (49), 105 (31); *anal*. C 50.19%, H 6.25%, calcd for $C_{33}H_{44}O_{19}$·5/2 H_2O, C 50.13%, H 5.91%. Acidic hydrolysis of **4** and TLC analysis in a manner similar to that described for **3** showed the presence of compound **1** and glucose in the products.

Phyllaemblicin C (5): yellowish amorphous powder; $[\alpha]^{25}_D$ +14.5° (c 0.52, MeOH); UV (MeOH) λ_{max} (log ϵ) 272 (3.20), 279 (3.12) nm; IR (KBr) ν_{max} 3349, 2931, 1779, 1711, 1603, 1452, 1279, 1171, 1073, 1027 cm^{-1}; ^{1}H NMR (CD_3OD, 500 MHz) δ aglycon: 8.18 (2H, dd, J = 7.5, 1.0 Hz, H-3′, 7′), 7.69 (1H, t, J = 7.5 Hz, H-5′), 7.57 (2H, t, J = 7.5 Hz, H-4′, 6′), 5.39 (1H, d, J = 3.0 Hz, H-10), 4.31 (1H, br s, H-5), 4.03 (1H, t, J = 11.0 Hz, H-12a), 3.94 (1H, br s, H-1), 3.57 (1H, br d, J = 11.0 Hz, H-12b), 2.93 (1H, tt, J = 13.5, 2.5 Hz, H-3), 2.45 (1H, dd, J = 13.5, 2.5 Hz, H-4a), 2.24 (1H, dd, J = 15.0, 3.0 Hz, H-9a), 2.18 (1H, m, H-11), 2.07 (1H, dd, J = 15.0, 3.0 Hz, H-9b), 1.99 (1H, dd, J = 13.5, 2.0 Hz, H-2a), 1.88 (1H, dt, J = 13.5, 3.5 Hz, H-4b), 1.79 (1H, dt, J = 13.5, 2.5 Hz, H-2b), 0.88 (3H, d, J = 7.0 Hz, H-14); inner glucose, 5.59 (1H, d, J = 8.5 Hz, glc H-1), 3.90 (1H, dd, J = 12.0, 2.5, glc H-6a), 3.76 (1H, dd, J = 12.0, 5.0 Hz, glc H-6b), 3.57 (1H, dd, J = 9.5, 9.0 Hz, glc H-3), 3.51 (1H, t, J = 9.0 Hz, glc H-4), 3.41 (1H, m, glc H-4), 3.31 (1H, dd, J = 8.5, 9.0 Hz, glc H-2), middle glucose: 4.14 (1H, d, J = 8.0 Hz, glc H-1), 3.46 (1H, dd, J = 12.0, 2.0 Hz, glc H-6a), 3.52 (1H, dd, J = 12.0, 4.0 Hz, glc H-6b), 3.37 (1H, m, glc H-5), 3.29 (1H, dd, J = 8.5, 9.0 Hz, glc H-4), 3.24 (1H, dd, J = 8.0, 9.5, glc H-2), 2.48 (1H, br t, J = 9.5 Hz, glc H-3); arabinose, 4.47 (1H, d, J = 7.0 Hz, ara H-1), 3.99 (1H, dd, J = 12.0, 3.0 Hz, ara H-5a), 3.64 (1H, ss, J = 9.0, 7.0 Hz, ara H-2), 3.63 (1H, br d, J = 12.0 Hz, ara H-5b), 3.57 (1H, br d, J = 9.0 Hz, ara H-3), 3.82 (1H, br s, ara H-4); ^{13}C NMR (CD_3OD, 125 MHz) δ 213.5 (C-7), 175.7 (C-13), 167.7 (C-1′), 134.5 (C-5′), 132.1 (C-2′), 130.9 (C-3′, 7′), 130.0 (C-4′, 6′), 100.5 (C-8), 76.3 (C-5), 75.4 (C-6), 71.5 (C-1), 70.8 (C-10), 63.3 (C-12), 34.3 (C-11), 32.8 (C-9), 32.1 (C-2, 3), 29.6 (C-4), 13.1 (C-14); inner glucose, 93.5 (glc C-1) 84.5 (glc C-2), 78.9 (glc C-5), 77.5 (glc C-3), 70.0 (glc C-4), 62.3 (glc C-6); middle glucose, 104.8 (glc C-1), 85.2 (glc C-2), 77.7 (glc C-5), 76.9 (glc C-5), 70.1 (glc C-4), 61.4 (glc C-6); arabinose, 107.2 (ara C-1), 74.0 (ara C-3), 73.7 (ara C-2), 69.5 (ara C-4), 67.7 (ara C-5); FABMS m/z 899 $[M + Na]^+$ (13), 877 $[M + H]^+$ (20), 583 (5), 421 (32); *anal*. C 48.56%, H 6.33%, calcd for $C_{38}H_{52}O_{23}$·7/2H_2O, C 48.41%, H 5.89%.

Acidic Hydrolysis of 5. A solution of **5** (10 mg) in 0.5 N H_2SO_4 (1 mL) was heated at 80 °C for 21 h. The mixture was neutralized with Amberlite IRA-400 (OH^- form) resin, concentrated *in vacuo*, and then chromatographed over Si gel with $CHCl_3$−MeOH−H_2O (7:3:0.5) to yield D-glucose [(3.9 mg) $[\alpha]^{25}_D$ +16.3° (c 0.3, H_2O), R_f 0.1 ($CHCl_3$−MeOH−H_2O, 7:3:0.5)] and L-arabinose [(2.1 mg), $[\alpha]^{25}_D$ +22.3° (c 0.16, H_2O), R_f 0.2 ($CHCl_3$−MeOH−H_2O, 7:3:0.5)].

Acetylation of 5. Compound **5** (32 mg) was treated with pyridine (1 mL) and Ac_2O (1 mL) at room temperature overnight. After concentration *in vacuo*, the residue was subjected to passage over a Si gel column to give **5a** (19.3 mg): white powder, $[\alpha]^{25}_D$ +20.8° (c 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (2H, dd, J = 8.0,1.0 Hz, H-3′, 7′), 7.58 (1H, tt, J = 1.0, 8.0 Hz, H-5′), 7.49 (2H, br t, J = 8.0 Hz, H-4′, 6′), 5.33 (1H, q, J = 3.0 Hz, H-10), 4.94 (1H, br s, H-1), 4.38 (1H, br s, H-5), 3.64 (1H, dd, J = 4.5,11.0 Hz, H-12b), 2.59 (1H, tt, J = 3.0, 12.5 Hz, H-3), 2.34 (1H, br d, J = 13.0 Hz, H-4a), 2.27 (1H, dd, J = 3.0, 15.0 Hz, H-9a), 2.24 (3H, s, CH_3CO-1), 2.23 (1H, m, H-11), 2.10 (1H, dd, J = 3.0, 15.0 Hz, H-9b), 2.07, 2.05, 2.01, 1.99 (each 6H, s, CH_3CO), 1.97 (3H, s, CH_3CO), 1.94−2.02 (2H, m, H-2a, 4b), 1.83 (1H, ddd, J = 2.5, 3.0, 15.0 Hz, H-2b), 0.97 (3H, d, J = 7.0 Hz, H-14); inner glucose, 5.69 (1H, d, J = 7.5 Hz, glc H-1), 5.20 (1H, dd, J = 9.5, 8.5 Hz, glc H-3), 5.00 (1H, dd, J = 9.5, 10.0 Hz, glc H-4), 4.31 (1H, dd, J = 4.5, 13.0 Hz, glc H-6a), 4.07 (1H, dd, J = 2.0, 13.0 Hz, glc H-6b), 3.99 (1H, ddd, J = 2.0, 4.5, 10.0 Hz, glc H-5), 3.85 (1H, dd, J = 7.5, 8.5 Hz, glc H-2); middle glucose, 5.06 (1H, dd, J = 9.0, 9.5 Hz, glc H-3), 4.84 (1H, dd, J = 9.0, 10.0 Hz, glc H-4), 4.60 (1H, d, J = 7.5 Hz, glc H-1), 4.26 (1H,

dd, J = 5.5, 12.5 Hz, glc H-6a), 4.03 (2H, m, H-12a, glc H-6b), 3.62 (1H, ddd, J = 3.0, 5.5, 10.0 Hz, glc H-5), 3.56 (1H, dd, J = 7.5, 9.5 Hz, glc H-2); arabinose, 5.17 (1H, dd, J = 3.5, 4.0 Hz, ara H-4), 5.15 (1H, dd, J = 7.5, 10.0 Hz, ara H-2), 4.91 (1H, dd, J = 3.5, 10.0 Hz, ara H-3), 4.46 (1H, d, J = 7.5 Hz, ara H-1), 4.04 (1H, dd, J = 4.0, 12.5 Hz, ara H-5a), 3.53 (1H, dd, J = 1.5, 12.5 Hz, ara H-5b).

Epigallocatechin-(2β→7,4β→8)-gallocatechin (prodelphinidin A-1) (6): tan amorphous powder; $[\alpha]^{16}_{D}$ +25.3° (*c* 0.4, MeOH); ^{1}H NMR (CD_3COCD_3, 300 MHz) δ 6.76 (2H, s, B ring H-2, 6), 6.61 (2H, s, B′ ring H-2, 6), 6.15 (1H, s, H-6′), 5.98, 6.07 (each 1H, d, J = 2.4 Hz, H-6, 8), 4.57 (1H, d, J = 9 Hz, H-2′), 4.20, 4.13 (each 1H, d, J = 3.3 Hz, H-3, 4), 4.13 (1H, m, H-3′), 3.05 (1H, dd, J = 16.5, 6 Hz, H-4′), 2.57 (1H, dd, J = 16.5, 9.3 Hz, H-4′); negative FABMS *m/z* 607 $[M-H]^-$; *anal.* C 54.17%, H 4.74%, calcd for $C_{30}H_{24}O_{14}\cdot 3H_2O$, C 54.38%, H, 4.56%.

Epicatechin-(4β→8)-gallocatechin (7): tan amorphous powder; $[\alpha]^{16}_{D}$ +17.0° (*c* 0.4, MeOH); ^{1}H NMR (CD_3COCD_3, 300 MHz) δ 6.99 (1H, br s, B ring H-2), 6.76 (1H, d, J = 8.1 Hz, B ring H-5), 6.71 (1H, dd, J = 8.1, 2.1 Hz, B ring H-6), 6.52 (2H, s, B′ ring H-2, 6), 6.03, 5.96 (each 1H, d, J = 2.4 Hz, H-6, 8), 5.97 (1H, s, H-6′), 5.06 (1H, br s, H-2), 4.64 (2H, br s, H-2′, 3′), 4.02 (1H, m, H-3′), 3.94 (1H, br s, H-4), 2.84 (1H, dd, J = 16.2, 5.4 Hz, H-4′), 2.58 (1H, dd, J = 16.5, 7.8 Hz, H-4′); negative FABMS *m/z* 593 $[M-H]^-$; *anal.* C 54.69%, H 5.04%, calcd for $C_{30}H_{26}O_{13}\cdot 3.5H_2O$, C 54.80%, H, 5.06%.

Thiolysis of 7. A mixture of **7** (1 mg), mercaptoethanol (0.2 mL), concentrated HCl (0.01 mL), and EtOH (0.5 mL) was heated at 50 °C for 1 h and analyzed by reversed-phase HPLC [Cosmosil 5C_{18}-AR (2.5 mm i.d. × 250 mm); gradient elution of 10%→20% (30 min) CH_3CN in 50 mM H_3PO_4]. The peaks corresponding to gallocatechin (7.84 min) and epicatechin 4-(2-hydroxyethyl)thio ether (28.4 min) were detected and confirmed by co-HPLC with authentic samples.

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