Tannins and Related Compounds. XCII.[1] Isolation and Characterization of Cyanogenic Ellagitannins, Aleurinins A and B, and a Related *O*-Glycosidic Ellagitannin, Aleurinin C, from *Aleurites fordii* HEMSLEY

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A chemical examination of the tannin ingredients in the leaves of the wood oil tree, *Aleurites fordii* HEMSLEY (Euphorbiaceae), has led to the isolation of three new ellagitannins named aleurinins A (4), B (5) and C (6), together with corilagin (1), geraniin (2) and chebulagic acid (3). On the basis of chemical and spectroscopic evidence, the structures of aleurinins A (4) and B (5) have been established as ellagitannins possessing a novel cyanopropylene alcohol glucoside core, while aleurinin C (6) has been characterized as an ellagitannin based on a hydroxyacetone glucoside core.

Keywords *Aleurites fordii*; wood oil tree; Euphorbiaceae; aleurinin A—C; ellagitannin; cyanopropylene alcohol glucoside; hydroxyacetone glucoside; hexahydroxydiphenic acid; dehydrohexahydroxydiphenic acid

Aleurites fordii HEMSLEY (Euphorbiaceae), a native of mainland China, is cultivated in Japan and Taiwan for the drying oil of the seed, used to prepare ointments and plasters. The leaves as well as the seeds are regarded as toxic and insecticidal.[2]

In the course of our screening program for tannins in Euphorbiaceous plants, we have found that the leaves and seeds of this plant contain abundant tannins. To elucidate the composition of the tannins, we have carried out a large-scale extraction of the leaves, and isolated new ellagitannins, aleurinins A (**4**) and B (**5**), containing a novel cyanogenic glycoside core and a related glycosidic ellagitannin, aleurinin C (**6**), together with three known ellagitannins (**1**—**3**). This paper deals with the isolation and structural elucidation of these compounds.

The water-soluble portion of the aqueous acetone extract was directly subjected to Sephadex LH-20 chromatography with the previously reported solvent system of water–methanol–acetone.[3] The tannin fractions thus obtained were further separated by chromatographies on Sephadex LH-20, Fuji-gel ODS-G3 and Bondapak C_{18}/Porasil B to yield six compounds (**1**—**6**). Among them, compounds **1**—**3** were found to be identical with corilagin,[4] geraniin[5] and chebulagic acid,[6] respectively, by comparisons of their physical and spectral data with those of authentic specimens.

The new tannin, aleurinin A (**4**), contained a nitrogen atom in the molecule as revealed by elemental analysis ($C_{38}H_{27}O_{23}N \cdot 5H_2O$) and by negative and positive fast atom bombardment mass spectroscopy (FAB-MS) [*m/z* 864 $(M-H)^-$ and 866 $(M+H)^+$].[7] The polyalcohol core of **4** was confirmed as glucose by complete acid hydrolysis. The ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectrum showed a pair of aromatic one-proton singlets at δ 6.94 and 6.62, suggestive of the presence of a 4,4′,5,5′,6,6′-hexahydroxydiphenoyl group, and also exhibited duplicated signal patterns [δ 6.50, 3/4H, s and δ 6.21, 1/4H, d, J= 1.5 Hz, olefinic H; δ 5.11, 3/4H, s and δ 5.86, 1/4H, d, J=1.5 Hz, benzylmethine H] characteristic of equilibrium forms of the six- and five-membered hemiacetal rings in a dehydrohexahydroxydiphenoyl ester group.[5] The glucose anomeric signal, usually observed downfield from δ 6.0 in most ellagitannins, appeared in the upper field (around δ 4.7). The most characteristic feature in the ^{1}H-NMR spectrum was the observation of *exo*-methylene signals at δ 6.27 and 6.13, both being split into triplets (J= 1.5 Hz) through long-range couplings with methylene protons.

When treated with *o*-phenylenediamine in an acidic medium, **4** yielded a phenazine derivative (**4a**) [negative FAB-MS *m/z*: 919 (M^-)[8]]. The ^{1}H- and ^{13}C-NMR spectra of **4a** were straightforward, and clearly indicated the presence of an oxygen-bearing methylene (δ 4.22 and 4.11, each 1H, dt, J=12, 1.5 Hz; δ 68.4, t). The small J-value (J=

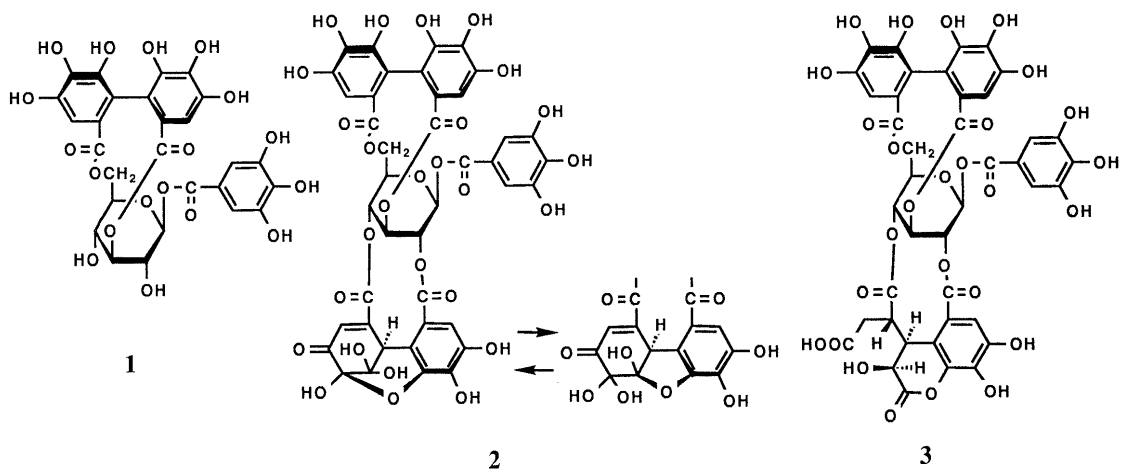


Chart 1

1.5 Hz) of these methylene signals was found by ^{1}H–^{1}H-shift correlation spectroscopy (COSY) to be due to a coupling with the *exo*-methylene signals at δ 5.44 and 5.74. The two-dimensional nuclear Overhauser enhancement (NOESY) spectrum of **4a** showed a cross peak between the sugar anomeric signal at δ 5.05 (d, J=6 Hz) and the methylene signals, thus suggesting that the methylene is linked to the sugar C-1 position.[9] Furthermore, a similar cross peak was observed between the sugar anomeric signal and the isolated aromatic singlet at δ 8.21 attributable to the proton on the quinoxaline ring. This fact implied that the quinoxaline ring is located at the glucose C-4 position, since examination of the Dreiding model showed that only in such a case is the anomeric proton close to the quinoxaline ring proton. In fact, the upfield shifts (δ 5.74 and 5.44, each 1H, t-like, J=1.5 Hz) of the aglycone *exo*-methylene signals on going from **4** to **4a**, rationalized in terms of the anisotropic effect of the quinoxaline ring, indicated that the glucose C-1 substituent is spatially close to the quinoxaline ring.

Methylation of **4a** with diazomethane, followed by alkaline methanolysis, yielded dimethyl hexamethoxydiphenoate (**4b**) and the phenazine tetramethoxy dimethyl ester (**4c**), which were found to be identical with authentic samples prepared from **2**. The positive sign of the specific optical rotations of **4b** (+29.9°) and **4c** (+37.4°) established the atropisomerism of the biphenyl bond to be in the *R*-series in both cases.[10] On the other hand, when heated in water, **4a** afforded a partial hydrolysate, whose physical and spectral data coincided with those of naturally-occurring aleurinin B (**5**). The ^{1}H-NMR spectrum of **5** exhibited a pair of aromatic singlets at δ 6.78 and 6.63 ascribable to the hexahydroxydiphenoyl ester group and no phenazine proton signal. The lowfield shifts of the glucose H-3 signal (δ 4.72, t, J=1.1 Hz) and one (δ 4.66, t, J=10.5 Hz) of the glucose H-6 signals, assigned by ^{1}H–^{1}H-COSY spectroscopy, indicated that the hexahydroxydiphenoyl ester is located at these positions.

The ^{13}C-NMR spectrum of **5** showed the anomeric signal at δ 101.5, the chemical shift clearly indicating the presence of an *O*-glycosidic linkage. Besides the hexahydroxydiphenoyl and glucose signals, four carbon signals (δ 67.7, 118.3, 133.0 and 120.8) arising from the aglycone moiety were observed. Among them, the former three were assigned to an oxygen-bearing methylene, sp^2-carbon and *exo*-methylene, respectively, based on ^{1}H–^{13}C-COSY spectroscopy, as well as consideration of the chemical shifts. On the other hand, taking into account the presence of a nitrogen atom in the molecule, the remaining signal at δ 120.8 was considered to be due to a nitrile carbon. All the FAB-MS data were consistent with the presence of the nitrile function, which was further confirmed by observation of the

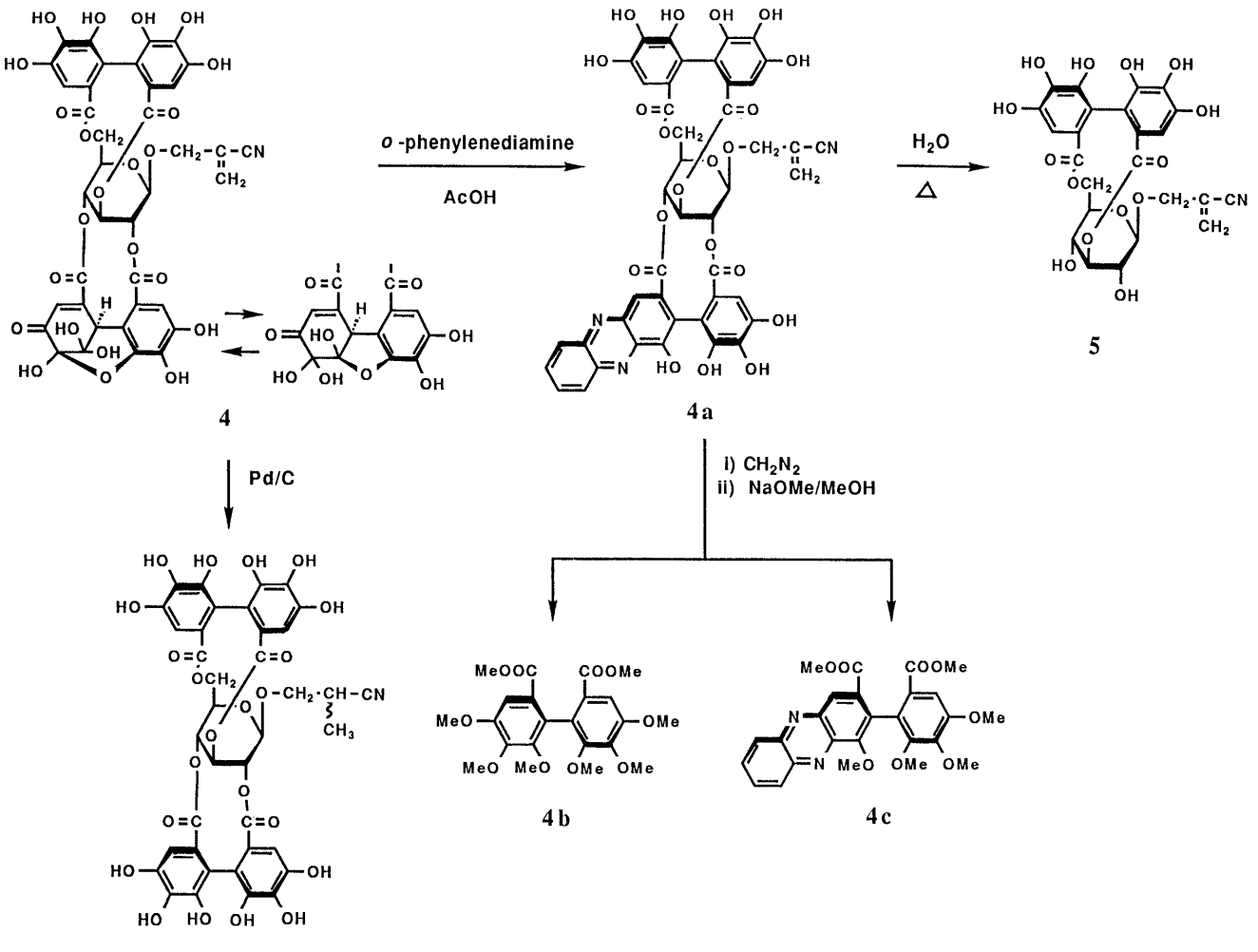
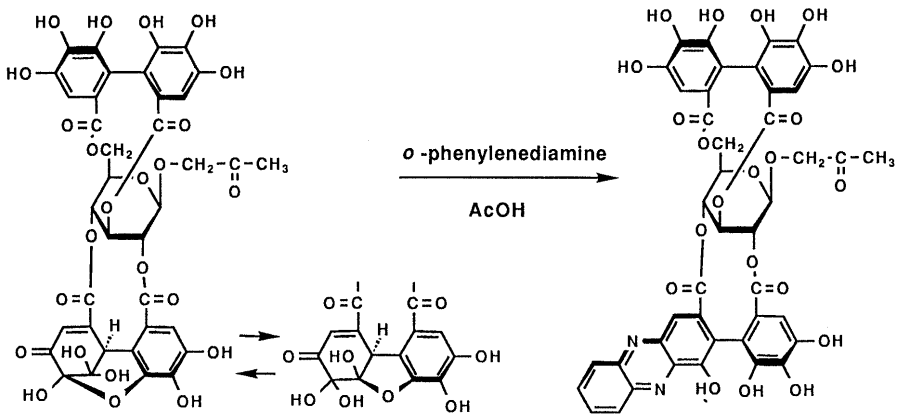


Chart 2



6 6a

Chart 3

infrared (IR) absorption band at 2230 cm^{-1} in **4**. Based on these findings, aleurinin B was characterized as an ellagitannin possessing a cyanopropylene alcohol glucoside core shown by the formula **5**.[11]

Consequently, the structure of aleurinin A was determined to be as represented by the formula **4**. It should be noted that hydrogenation of aleurinin A over palladium–carbon afforded a mixture of two diastereoisomers (**4d** and **4e**), which could not be separated by ordinary chromatography.

The ^{1}H- and ^{13}C-NMR spectra of aleurinin C (**6**) were duplicated owing to the existence of an equilibrium mixture of five- and six-membered hemiacetal compounds analogous to those of **2** and **4**. Acid-catalyzed condensation of **6** with *o*-phenylenediamine afforded the phenazine derivative (**6a**). The ^{1}H-NMR spectrum of **6a** was closely correlated with that of **4a**, the aromatic signal pattern and the coupling constants of the sugar signals being almost identical. However, the *exo*-methylene signals observed in **4a** were replaced by a methyl signal appearing at δ 1.69 as a singlet. The ^{13}C-NMR spectrum of **6a** was also similar to that of **4a**, except for the absence of the *exo*-methylene and sp^2-carbon signals and the appearance in their place of a methyl signal at δ 26.0 and a carbonyl signal at δ 206.3. The almost identical chemical shifts of the sugar signals indicated the polyalcohol core to be glucose and also the substitution system in the glucose moiety to be the same as in the case of **4a**. Since the presence of an isolated oxygen-bearing methylene was evident from both the ^{1}H- and ^{13}C-NMR spectra (δ 4.14 and 3.91, each 1H, d, J=17 Hz; δ 73.9), the aglycone moiety was concluded to be hydroxyacetone, in agreement with all the FAB-MS data [**6**: positive FAB-MS *m/z*: 857 $(M+H)^+$ and negative FAB-MS *m/z*: 855 $(M-H)^-$; **6a**: negative FAB-MS *m/z*: 910 (M^-)[8]]. On the basis of these chemical and spectroscopic data, the structure of aleurinin C was determined to be as shown by the formula **6**.[11]

Aleurinins A and C represent the first examples of *O*-glycosidic ellagitannins which possess the dehydrohexahydroxydiphenoyl ester group. The fact that hydrolyzable tannins having an *O*-glycopyranoside core rarely occur in Nature suggests that the sugar C-1 position is, in most cases, galloylated at an earlier biosynthetic stage than those of other positions. From this point of view, aleurinins are considered to be formed biosynthetically from a simple cyanopropylene alcohol glucoside or a hydroxyacetone glucoside, followed by acylation.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. FAB-MS were taken with a JEOL JMS DX-300 instrument. IR spectra were obtained with a JASCO IR-G spectrometer. ^{1}H- and ^{13}C-NMR spectra were taken with JEOL FX-100, JEOL GX-270 and JEOL GX-400 spectrometers, with tetramethylsilane as an internal standard, and chemical shifts are given in δ (ppm). Column chromatography was carried out with Sephadex LH-20 (25—100 μ, Pharmacia Fine Chemical Co., Ltd.), MCI-gel CHP-20P (75—150 μ, Mitsubishi Chemical Industries, Ltd.), Fuji-gel ODS-G3 (43—65 μ, Fuji-Gel Hanbai Co., Ltd.), Bondapak C_{18}/Porasil B (37—75 μ, Waters Associates, Inc.) and Kieselgel 60 (70—230 mesh, Merck). Thin-layer chromatography (TLC) was conducted on precoated Kieselgel 60 F_{254} plates (0.2 mm thick, Merck) and precoated cellulose F_{254} plates (0.1 mm, Merck) with solvent systems of benzene–ethyl formate–formic acid (Kieselgel; 2:7:1, 1:7:1, 1:5:2, cellulose; 2% acetic acid (for phenolics) and benzene–acetone (for acetates and methyl ethers), and spots were located by ultraviolet illumination (Manasul light 2536 Å) and by spraying the ferric chloride reagent or 10% sulfuric acid followed by heating.

Extraction and Isolation The fresh leaves (11.2 kg) of *A. fordii*, collected in the Kasuya Experimental Forest of Kyushu University, were extracted five times at room temperature with 80% aqueous acetone. The combined extracts were concentrated under reduced pressure at *ca.* 40 °C to give dark brown precipitates, which were removed by filtration. The filtrate was further concentrated and applied to a Sephadex LH-20 column. After washing of the column with water, gradient elution with water containing increasing amounts of methanol and finally with water–acetone (1:1) furnished four fractions, among which the last two fractions contained tannins. The third fraction consisted mainly of corilagin (**1**), and was further chromatographed on MCI-gel CHP-20P with a mixture of water and methanol (4:1) to give **1**. Chromatography of the last fraction over MCI-gel CHP-20P with water containing increasing proportions of methanol yielded two fractions. The first fraction was repeatedly chromatographed over Sephadex LH-20 with ethanol and Fuji-gel ODS-G3 and Bondapak C_{18}/Porasil B with a mixture of water and methanol to furnish geraniin (**2**), chebulagic acid (**3**) and aleurinins A (**4**), B (**5**) and C (**6**). The second fraction was subjected to Sephadex LH-20 chromatography with ethanol and then with 80% aqueous methanol to afford a further crop of **1**. The total yields were as follows; corilagin (**1**) (2.69 g), geraniin (**2**) (4.15 g), chebulagic acid (**3**) (21 mg), aleurinin A (**4**) (1.44 g), aleurinin B (**5**) (35 mg) and aleurinin C (**6**) (187 mg).

Aleurinin A (4) A yellow amorphous powder, $[\alpha]_D^{18}$ −65.0° (c=0.65, MeOH). *Anal.* Calcd for $C_{38}H_{27}NO_{23}\cdot 5H_2O$: C, 47.76; H, 3.90; N, 1.47. Found: C, 47.65; H, 3.57; N, 1.38. Negative FAB-MS *m/z*: 864 $(M-H)^-$. Positive FAB-MS *m/z*: 866 $(M+H)^+$, 783 $[M-HOCH_2C(CN)=CH_2+H]^+$. IR ν_{max}^{KBr} cm^{-1}: 3370 (OH), 2230 (CN), 1730, 1700 (–COO–), 1615 (aromatic H). ^{1}H-NMR (acetone-d_6, 100 MHz): 7.26 (1/4H, DHHDP-

H^{12}), 7.22 (3/4H, DHHDP-H), 6.94, 6.62 (each 1H, s, HHDP-H^{12}), 6.50 (3/4H, s, DHHDP-H), 6.27 (1H, t, J=1.5 Hz, =CH_2), 6.21 (1/4H, d, J=1.5 Hz, DHHDP-H), 6.13 (1H, t, J=1.5 Hz, =CH_2), 5.47, 5.37, 5.28 (3H in total, each br s, glc-2,3,4-H), 5.11 (3/4H, s, DHHDP-H), 5.86 (1/4H, d, J=1.5 Hz, DHHDP-H), 4.76—4.31 (6H, m, glc-1,5,6-H and –OCH_2–). ^{13}C-NMR (acetone-d_6, 25.05 MHz): 46.0 (DHHDP-C), 51.8 (DHHDP-C), 63.9, 66.4, 67.4, 67.9, 70.8, 71.8, 72.5, 73.4 (glc-2,3,4,5,6-C and –OCH_2–), 92.4 (DHHDP-C), 96.1 (DHHDP-C), 97.7, 98.2 (glc-1-C), 107.8 (HHDP-C), 109.0 (DHHDP-C), 110.0 (HHDP-C), 113.5, 115.0 (DHHDP-C), 115.7, 116.4 (HHDP-C), 117.6 (CN or –C=CH_2), 119.3, 119.7, 119.9 (C=CH_2 or CN, DHHDP-C), 124.6, 125.8 (HHDP-C), 125.6, 128.5 (DHHDP-C), 133.5 (C=CH_2), 136.2, 137.1 (HHDP-C), 138.9, 143.2, 147.5, 149.2, 154.5 (DHHDP-C), 164.7, 165.4, 165.6, 166.2, 168.1 (–COO–), 191.8, 194.5 (DHHDP-C).

Formation of the Phenazine (4a) A mixture of **4** (206 mg) and *o*-phenylenediamine (28 mg) in 10% ethanolic acetic acid (0.6 ml) was left standing at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure, and the residue was chromatographed over Sephadex LH-20. Elution with ethanol containing increasing amounts of methanol yielded the phenazine derivative (**4a**) as a tan amorphous powder (101 mg), $[\alpha]_D^{22}$ −12.8° (c=0.14, MeOH). *Anal.* Calcd for $C_{44}H_{29}N_3O_{20}\cdot 4H_2O$: C, 53.28; H, 3.76; N, 4.24. Found: C, 52.98; H, 3.90; N, 3.95. Negative FAB-MS m/z: 919 (M^-). ^{1}H-NMR (acetone-d_6, 100 MHz): 8.37—8.20 (2H, m, Ph-H-4″,5″), 8.21 (1H, s, Ph-H-3), 7.51 (1H, s, Ph-H-3′), 8.07—7.94 (2H, m, Ph-H-3″,6″), 6.90, 6.67 (1H, s, HHDP-H), 5.74 (1H, t-like, J=1.5 Hz, =CH_2), 5.44 (1H, t-like, J=1.5 Hz, =CH_2), 5.40, 5.39, 5.33 (3H, m, glc H-2,3,4), 5.05 (1H, d, J=6 Hz, glc H-1), 4.94 (1H, dd, J=2, 8 Hz, glc H-5), 4.77 (1H, dd, J=8, 11 Hz, glc H-6), 4.22 (1H, dt, J=12, 1.5 Hz, –OCH_2–), 4.11 (1H, dt, J=12, 1.5 Hz, –OCH_2–), 3.98 (1H, dd, J=2, 11 Hz, glc H-6). ^{13}C-NMR (acetone-d_6, 25.05 MHz): 65.6 (glc C-6), 67.9 (glc C-4), 68.4 (–OCH_2–), 69.1 (glc C-2), 76.5 (glc C-5), 77.3 (glc C-3), 97.7 (glc C-1), 108.1, 109.3 (HHDP-C-3,3′), 113.3 (Ph-C-3′), 115.1, 116.5, 116.7, 117.1, 117.5 (Ph-C-1, 1′, HHDP-C-1,1′ and CN or C=CH_2), 119.8, 119.9 (×2) (Ph-C-3,2′ and C=CH_2 or CN), 124.2, 125.2 (HHDP-C-2,2′), 130.1, 130.2 (Ph-C-4″,5″), 132.5 (×2) (Ph-C-3″,6″), 133.5 (C=CH_2), 136.1 (Ph-C-2), 137.2, 139.1 (×2), 139.5 (Ph-C-5,5′ and HHDP-C-5,5′), 142.7, 142.9 (Ph-1″,2″), 144.9, 145.0 (×2), 145.3 (×3), 145.7 (HHDP-C-4,4′,6,6′ and Ph-C-3,4′,6′), 152.0 (Ph-C-6), 166.4 (×2), 168.0, 168.9 (–COO–).

Methylation of 4a, Followed by Alkaline Methanolysis A solution of **4a** (131 mg) in methanol was treated with ethereal diazomethane at 0 °C for 2 h. After evaporation of the solvent, the residue was similarly treated with diazomethane. The reaction product was separated by silica gel chromatography with benzene–acetone to yield the methyl ether (91 mg), which was methanolyzed with 2% sodium methoxide in methanol at room temperature overnight. The reaction mixture was neutralized with Amberlite IR-120B (H^+ form) resins and applied to a silica gel column. Elution with benzene containing increasing proportions of acetone gave *R*-dimethyl hexamethoxydiphenoate (**4b**) as a colorless syrup (23 mg), $[\alpha]_D^{14}$ +29.9° (c=0.6, $CHCl_3$) and the phenazine tetramethoxy dimethyl ester (**4c**) as a pale yellow syrup (19 mg), $[\alpha]_D^{14}$ +37.4° (c=0.4, $CHCl_3$).

Hydrogenation of 4 A solution of **4** (70 mg) in ethanol (5 ml) was hydrogenated over 5% palladium–carbon overnight. After removal of the catalyst by filtration, the solution was concentrated to dryness. The residue was chromatographed over Bondapak C_{18}/Porasil B with a mixture of water and methanol to afford the products (**4d** and **4e**) as an off-white amorphous powder, $[\alpha]_D^{15}$ +23.4° (c=0.8, MeOH). Negative FAB-MS m/z: 850 ($M-H)^-$. Positive FAB-MS m/z: 852 $(M+H)^+$, 460. ^{1}H-NMR (acetone-d_6, 100 MHz): 7.39, 6.89, 6.87, 6.62 (each 1H, s, HHDP-H), 5.33 (1H, d, J=4 Hz, glc H-2), 5.22 (1H, d, J=6 Hz, glc H-4 or H-3), 5.14 (1H, br d, J=4 Hz, glc H-1), 5.01 (1H, br d, J=6 Hz, glc H-3 or H-4), 4.73—4.59 (2H, m, glc H-5, 6), 4.07—3.39 (4H, m, glc H-6, –OCH_2CH–), 1.20, 1.17 (each 3/2H, d, J=7 Hz, CH_3).

Partial Hydrolysis of 4a A solution of **4a** (73 mg) in water (3 ml) and methanol (3 ml) was heated under reflux for 10 h. After cooling, the solvent was evaporated off under reduced pressure, and the residue was subjected to MCI-gel CHP-20P chromatography with a mixture of water and methanol to furnish the product (27 mg), which was found to be identical with aleurinin B (**5**) by comparison of specific optical rotation and ^{1}H-NMR spectrum.

Aleurinin B (5) An off-white amorphous powder, $[\alpha]_D^{15}$ −89.7° (c=0.3, MeOH). *Anal.* Calcd for $C_{24}H_{21}NO_{14}\cdot 2H_2O$: C, 49.28; H, 4.31; N, 2.39. Found: C, 48.85; H, 4.35; H, 2.26. Negative FAB-MS m/z: 546 ($M-H)^-$. ^{1}H-NMR (acetone-d_6, 400 MHz): 6.78, 6.63 (each 1H, s, HHDP-H), 6.19, 6.06 (each 1H, t, J=1.8 Hz, C=CH_2), 5.03 (1H, d, J=1.8 Hz, glc H-1), 4.72 (1H, t, J=1.1 Hz, glc H-3), 4.66 (1H, t, J=10.5 Hz, glc H-6), 4.44 (1H, d, J=13.9 Hz, –OCH_2–), 4.41—4.38 (2H, m, glc H-4, 5), 4.25 (1H, dd, J=1.5, 13.9 Hz, –OCH_2–), 4.19 (1H, dd, J=7.7, 10.5 Hz, glc H-6), 3.97 (1H, br t, J=1.8 Hz, glc H-2). ^{13}C-NMR (acetone-d_6, 100 MHz): 62.9 (glc C-4), 64.6 (glc C-6), 67.7 (–OCH_2–), 70.3 (glc C-2), 71.0 (glc C-3), 75.8 (glc C-5), 101.5 (glc C-1), 108.2, 110.0 (HHDP-C-3,3′), 116.1, 116.8 (HHDP-C-1,1′), 118.3 (C=CH_2), 120.8 (CN), 126.3, 126.5 (HHDP-C-2,2′), 133.0 (C=CH_2), 136.7, 137.2 (HHDP-C-5,5′), 145.4, 145.8 (HHDP-C-4,4′,6,6′), 167.7, 168.6 (–COO–).

Acetylation of 5 A solution of **5** (62 mg) in acetic anhydride (2 ml) and dry pyridine (0.2 ml) was kept at room temperature overnight. The reaction mixture was poured into ice water, and resulting white precipitates were collected by filtration. Purification by silica gel chromatography with benzene-acetone gave the octaacetate as a white amorphous powder (19 mg), $[\alpha]_D^{15}$ −5.3° (c=0.3, $CHCl_3$). Positive FAB-MS m/z: 884 $(M+H)^+$. ^{1}H-NMR ($CDCl_3$, 100 MHz): 7.63, 7.57 (each 1H, s, HHDP-H), 6.06, 6.02 (each 1H, t, J=1.5 Hz, C=CH_2), 5.35 (1H, br d, J=3 Hz, glc H-3), 5.13 (1H, br d, J=4 Hz, glc H-1), 3.92 (1H, br s, glc H-4), 3.86 (1H, d, J=4 Hz, glc H-2), 3.70—3.30 (3H, m, glc H-5,6), 3.40 (1H, d; J=13 Hz, –OCH_2), 3.12 (1H, br d, J=13 Hz, –OCH_2), 2.32, 2.28, 2.26 (×2), 2.14, 2.09, 2.03, 1.98 (each 3H, s, –$OCOCH_3$).

Aleurinin C (6) A yellow amorphous powder, $[\alpha]_D^{22}$ −23.5° (c=0.24, MeOH). *Anal.* Calcd for $C_{38}H_{28}O_{24}\cdot 4H_2O$: C, 47.85; H, 3.91. Found: C, 47.93; H, 4.26. Negative FAB-MS m/z: 855 ($M-H)^-$. Positive FAB-MS m/z: 857 $(M+H)^+$, 783 $(M-OCH_2COCH_3)^+$. ^{1}H-NMR (acetone-d_6, 100 MHz): 7.27 (3/5H, s, DHHDP-H-3′), 7.25 (2/5H, s, DHHDP-H-3′), 6.95, 6.93, 6.62, 6.61 (2H in total, each s, HHDP-H), 6.50 (2/5H, DHHDP-H-3), 6.21 (3/5H, d, J=1.5 Hz, DHHDP-H-3), 5.28—5.23 (4H, m, glc H-1,2,3,4), 5.15 (2/5H, s, DHHDP-H-1), 4.87 (3/5H, d, J=1.5 Hz, DHHDP-H-1), 4.80—4.40 (3H, m, glc H-5,6), 4.39—4.32 (2H, m, –OCH_2–), 2.20, 2.17 (6/5H, and 9/5H, each s, OCH_3).

Formation of the Phenazine (6a) A mixture of **6** (100 mg) and *o*-phenylenediamine (15 mg) in 10% ethanolic acetic acid (1.5 ml) was stirred at room temperature for 2 h. The reaction mixture was worked up as described for **4** to give the phenazine (**6a**) as a tan amorphous powder (50 mg), $[\alpha]_D^{21}$ −30.5° (c=0.12, MeOH). *Anal.* Calcd for $C_{43}H_{30}N_2O_{21}\cdot 4H_2O$: C, 52.55; H, 3.90; N, 2.85. Found: C, 52.39; H, 4.01; N, 2.71. Negative FAB-MS m/z: 910 (M^-). ^{1}H-NMR (acetone-d_6+D_2O, 100 MHz): 8.36—8.19 (2H, m, Ph H-4″,5″), 8.19 (1H, s, Ph H-3), 8.05—7.95 (2H, m, Ph H-3″,6″), 7.49 (1H, s, Ph H-3′), 6.93, 6.69 (each 1H, s, HHDP-H), 5.44—5.34 (3H, m, glc H-2,3,4), 5.01 (1H, d, J=6 Hz, glc H-1), 4.93 (1H, dd, J=3, 8 Hz, glc H-5), 4.76 (1H, t, J=8 Hz, glc H-6), 4.14 (1H, d, J=17 Hz, –OCH_2–), 3.96 (1H, dd, J=3, 8 Hz, glc H-6), 3.91 (1H, J=17 Hz, –OCH_2–), 1.69 (3H, s, OCH_3). ^{13}C-NMR (acetone-d_6+D_2O): 26.0 (CH_3), 65.7 (glc C-6), 67.7 (glc C-4), 69.0 (glc C-2), 73.9 (–OCH_2–), 76.5 (glc C-5), 77.6 (glc C-3), 98.9 (glc C-1), 108.3, 109.3 (HHDP-C-3,3′), 113.3 (Ph C-3′), 115.2 (Ph C-1′), 116.4, 116.6 (HHDP-C-1,1′), 117.5 (Ph C-1), 119.8, 120.0 (Ph C-2′), 124.3, 125.2 (HHDP-C-2,2′), 129.9, 130.2 (Ph C-4″,5″), 132.4 (×2) (Ph C-3″,6″), 136.0, 136.2, 137.2, 139.1 (×2), 139.5 (Ph C-2,4,5,5′ and HHDP-C-5,5′), 142.6 (Ph C-1″,2″), 144.7, 145.1, 145.3, 145.7 (HHDP-C-4,4′,6,6′ and Ph C-4′,6′), 151.9 (Ph C-6), 166.6 (×2), 168.1, 169.0 (–COO–).

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