Tannins and Related Compounds. C.[1] Reaction of Dehydrohexahydroxydiphenic Acid Esters with Bases, and Its Application to the Structure Determination of Pomegranate Tannins, Granatins A and B

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Some novel reactions of dehydrohexahydroxydiphenic acid esters [*e.g.*, geraniin (1)] with bases are presented. Namely, treatment of 1 with triethylamine or sodium benzenesulfinate in acetonitrile caused a benzylic acid-type rearrangement to yield a brevifolin carboxylic acid derivative (3). On the other hand, treatment of 1 with pyridine gave a tetrahydroxydibenzofuran derivative (8), whereas reaction with aqueous sodium hydroxide cleaved the carbon–carbon linkage to yield a dehydrochebulic acid ester (10).

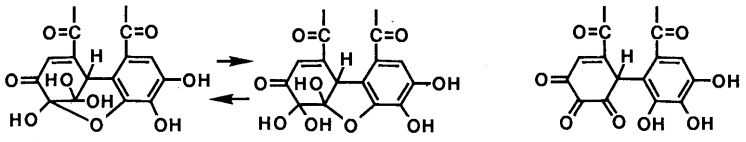
The application of these reactions to granatins A and B, the major tannins in pomegranate, unequivocally established their structures (13 and 11, respectively).

Keywords dehydrohexahydroxydiphenic acid; geraniin; base-catalyzed rearrangement; base-catalyzed degradation; brevifolincarboxylic acid; tetrahydroxydibenzofuran dicarboxylic acid; dehydrochebulic acid; granatin A; granatin B; tannin

During the past decade, much progress has been made in elucidating the chemistry of vegetable tannins, and particularly in the field of hydrolyzable tannins, many compounds having a variety of component phenolcarboxylic acids have been isolated and structurally elucidated. The accumulated structural studies have now shown that most of these acid esters are formed biosynthetically *via* 3,3′,4,4′,5,5′-hexahydroxydiphenoyl esters (originating from gallic acid esters) by oxidation and/or phenol coupling.[2] Furthermore, our extensive chemical work revealed that among others, tannins (*e.g.*, geraniin (**1**),[3] mallotusinic acid (**2**),[4] *etc.*) possessing a dehydrohexahydroxydiphenoyl group[3,5] (Chart 1) occur widely in the plant kingdom, especially in members of the families Euphorbiaceae,[6] Cercidiphyllaceae,[7] Elaeocarpaceae,[8] Simaroubaceae[9] and Punicaceae.[10] This dehydrohexahydroxydiphenic acid is considered from its structural features to be formed by a simple phenolic oxidation of the hexahydroxydiphenic acid, and is structurally unique in that it contains a hydrated cyclohexenetrione moiety. There has, however, been no systematic reaction study on this acid ester, except for the phenazine formation[5] and reduction leading to the hexahydroxydiphenoyl ester.[11] In this paper, we wish to report some significant findings obtained by the reaction of dehydrohexahydroxydiphenoyl glucose derivatives [mainly geraniin (**1**)] with bases, and also to describe the structure determination of granatins A (**13**) and B (**11**), the major tannins in pomegranate (*Punica granatum* L.), by application of the newly found reactions.

Since the dehydrohexahydroxydiphenoyl glucoses[12] have phenolic hydroxyl groups and ester bonds which are extremely unstable to strong bases and acids, the allowable reaction conditions are restricted, and therefore we first examined the action of the weak base, triethylamine. When the yellow compound, geraniin (**1**), which is the major tannin in most species of Euphorbiaceae,[6] Simaroubaceae[9] and Geraniaceae,[3] was treated with triethylamine in acetonitrile, a variety of products were formed, among which a major compound (**3**) (33%[13]) was isolated by a combination of MCI gel CHP 20P and Sephadex LH-20 chromatographies. The negative fast atom bombardment mass spectrum (FAB-MS)[14] [*m/z*: 907 $(M-H)^-$] of **3** indicated the loss of carbon dioxide (−44 m.u.). The ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectrum exhibited, besides signals arising from one galloyl group [δ 7.20 (2H, s)] and one hexahydroxydiphenoyl group [δ 6.89, 6.67 (1H, each s)] and from the glucopyranose moiety, an aromatic singlet (δ 7.47) and aliphatic ABX-type signals [δ 4.67 (overlapped with the glucose H-5 signal), 3.12 (dd, J=7, 18 Hz) and 2.71 (dd, J=2, 19 Hz)], the chemical shifts and coupling patterns being analogous to those of brevifolincarboxylic acid (**4**).[15] The presence of the brevifolincarboxylic acid moiety was further confirmed by acid hydrolysis of **3**, which yielded **4**, together with corilagin (**5**).[10a,16] The location of the brevifolincarboxyl ester was readily determined to be at C-4 on the basis of the remarkable upfield shift of the H-2 signal (δ 4.26), compared with that of the parent compound (**1**) (δ 5.58). From these findings, the structure of the product **3** was established to be 1-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenoyl-4-*O*-brevifolincarboxyl-β-D-glucopyranose (**3**).[17]

On treatment of geraniin (**1**) with sodium benzenesulfinate in acetonitrile, a similar reaction occurred to yield **3** (3%) and a new product (**6**) (12%). The ^{1}H- and ^{13}C-NMR spectra of **6** were similar to those of **3**, except for the lowfield shift of the glucose H-2 signal [δ 5.38 (dd, J=1, 3 Hz)], thus indicating the location of the acyl group at the C-2 position. The negative FAB-MS [*m/z*: 907 $(M-H)^-$] was



hydrated forms

dehydrohexahydroxydiphenoyl group

Chart 1

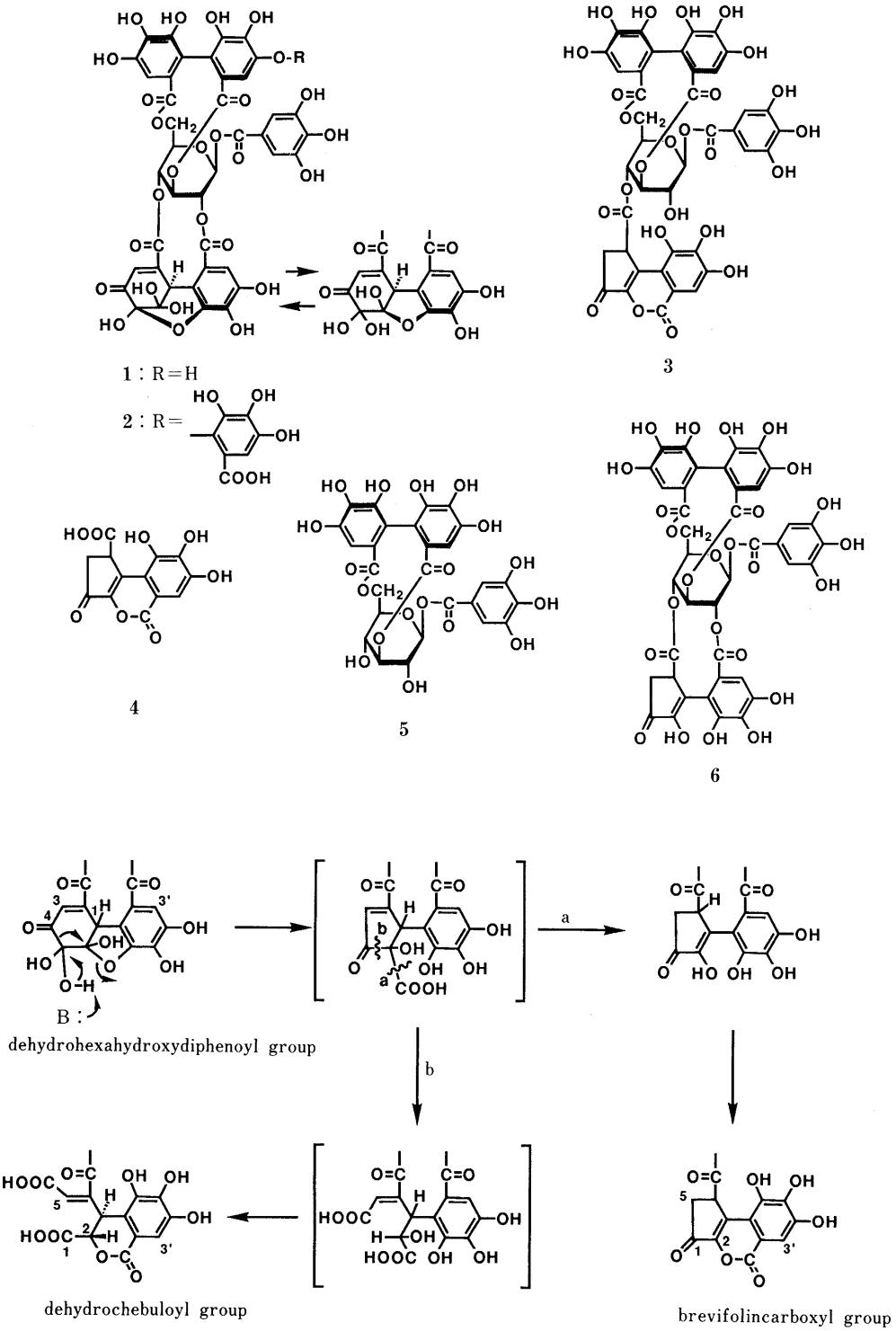
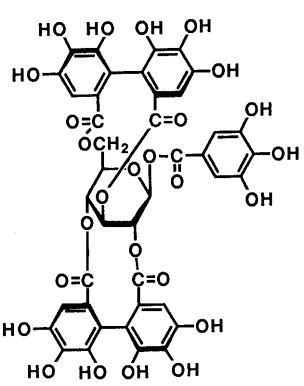


Chart 2. Possible Reaction Mechanism

in agreement with the proposed structure (**6**). Furthermore, the fact that the reaction at higher temperature decreased the yield of **5** and instead increased the yield of **3** (27%) also supported the structure (**6**).

The mechanism of these reactions can be well explained by a benzylic acid-type rearrangement, followed by decarboxylation (Chart 2, route a).[12] This type of reaction also proceeded in the presence of water, although addition of excess water decreased the yield of **3** because of the hydrolysis of the ester bond. The use of much stronger bases such as 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) and diisopropylethylamine gave complex mixtures. It should be noted that prolonged treatment with triethylamine caused epimerization at the methine carbon bearing a carboxyl group.

In contrast to the aliphatic amines, aromatic amines react with the dehydrohexahydroxydiphenoyl ester group in a different way. Treatment of geraniin (**1**) with pyridine in acetonitrile gave four products, of which two minor ones were readily identifiable as corilagin (**5**) (5%) and compound **3** (4%). The others were found to be reduction products, which were identical with 1-*O*-galloyl-2,4;3,6-bis-(*R*)-hexa-



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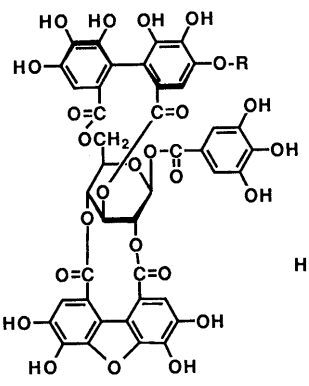
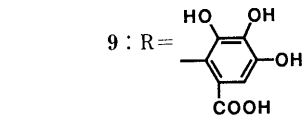
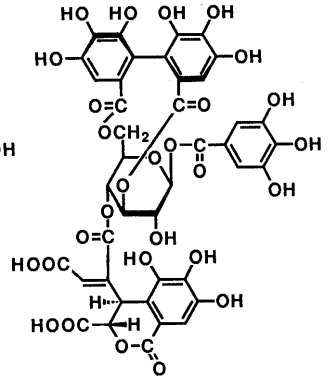


8 : R=H

9 : R=





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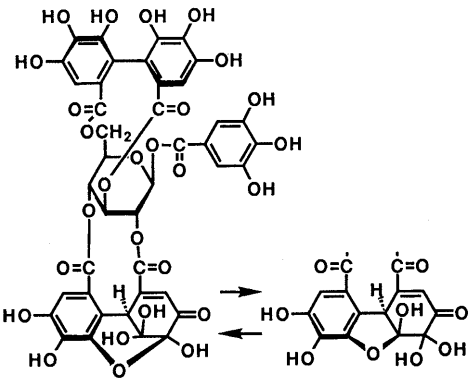

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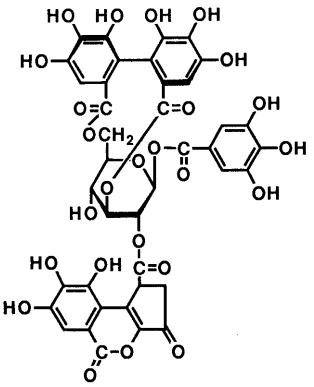

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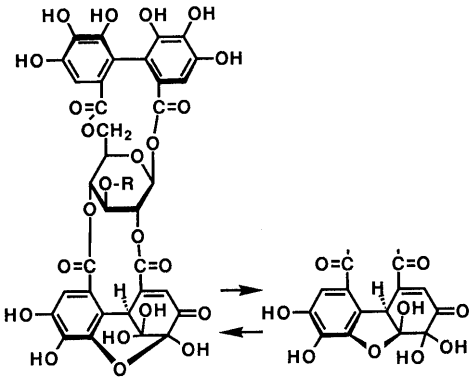
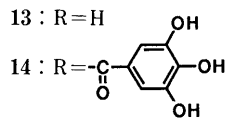
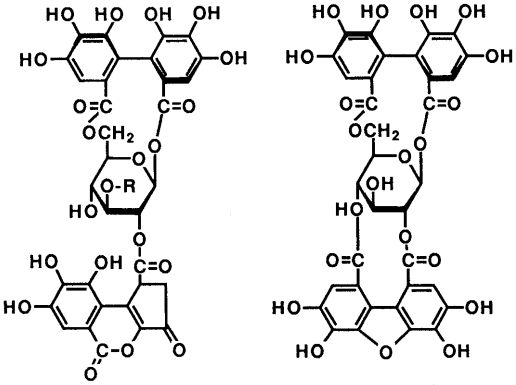


13 : R=H

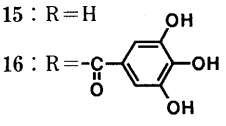
14 : R=





15 : R=H

16 : R=



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hydroxydiphenoyl-β-D-glucose (**7**)[11b] (1.7%) and 1-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenoyl-2,4-tetrahydroxydibenzofurandicarboxyl-β-D-glucose (**8**) (35.4%), the latter having recently been isolated from the bark of *Mallotus japonicus*.[4] The production of **8** can probably be explained by redox disproportionation,[12] although oxidation products could not be isolated. A similar reaction also occurred when 2,6-lutidine was used instead of pyridine.

Brief heating of geraniin (**1**) in aqueous sodium hydroxide (pH 9, 5 min) yielded a product, which was found to be identical with repandusinic acid A (**10**)[15] (17%), along with **3** (12%) and corilagin (**5**) (17%). The dehydrochebuloyl ester in **10** was considered to have been formed *via* the benzylic acid-type rearrangement, followed by cleavage of the carbon–carbon bond and *trans*-isomerization of the double bond (Chart 2, route b).[12]

The reactions found in this study were applied to the determination of the orientation of the dehydrohexahydroxydiphenoyl group in granatins B (**11**) and A (**13**), whose structures were formerly proposed to be 1-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenoyl-2,4-(*S*)-dehydrohexahydroxydiphenoyl-β-D-glucose[10b,11b] and 1,6-(*S*)-hexahydroxydiphenoyl-2,4-(*S*)-dehydrohexahydroxydiphenoyl-β-D-glucose,[10c,11b] respectively, but the orientation of the dehydrohexahydroxydiphenoyl group remained to be clarified.

When treated with triethylamine in acetonitrile, granatin B (**11**) yielded a product **12** (21%), whose ^{1}H- and ^{13}C-NMR spectra were closely related to those of **3**, except for the chemical shifts of the glucopyranose protons; the signal due to H-2 was observed at lower field (δ 5.19, br d, J=4 Hz), whereas the H-4 signal was shifted to higher field (δ 4.39, d, J=3 Hz), indicating that the brevifolincarboxyl group is located at the C-2 hydroxyl group. Hence, the product was characterized as 1-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenoyl-2-*O*-brevifolincarboxyl-β-D-glucose (**12**). This result led to the conclusion that the orientation of the dehydrohexahydroxydiphenoyl group can be represented by the formula **11**.

Similar treatment of granatin A (**13**) with triethylamine afforded a product (**15**) (15%), whose ^{1}H- and ^{13}C-NMR spectra exhibited signals arising from the brevifolincarboxyl group. The upfield shift of the H-4 signal [δ 3.91 (t, J=6 Hz)] indicated that the brevifolincarboxyl ester is located at the C-2 hydroxyl group. Therefore the structure of granatin A should be represented by the formula **13**.

Although only the reaction of geraniin (**1**), as a representative of hydrolyzable tannins having a dehydrohexahydroxydiphenoyl group, has so far been described herein, other tannins such as mallotusinic acid (**2**) and helioscopinin A (**14**)[6c] afforded similar products; the details are described in Experimental.

Experimental

Melting points were determined with a Yanaco 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-HX 100/JMA 3500 data system using acetone/glycerol or hexamethylphosphoric triamide/glycerol as the matrix. ^{1}H- and ^{13}C-NMR spectra were recorded on JEOL FX-100 and GX-270 spectrometers using tetramethylsilane as an internal standard, and chemical shifts are given on the δ-scale. Column chromatography was carried out with Sephadex LH-20 (25—150 μ, Pharmacia Fine Chemical Co., Ltd.), MCI-gel CHP 20P (75—150 μ, Mitsubishi Chemical Industries, Ltd.) and Bondapak C_{18}/Porasil B (37—75 μ, Waters Associates, Inc.). Thin-layer chromatography (TLC) was conducted on precoated Kieselgel 60 F_{254} plates (0.2 mm thick, Merck) with benzene–ethyl formate–formic acid (2:7:1 or 1:7:1) and precoated cellulose F_{254} plates (0.1 mm, Merck) with 2% acetic acid, and spots were located by ultraviolet illumination (Manasul light 2536 Å) and by spraying the ferric chloride reagent or 10% sulfuric acid reagent, followed by heating.

Treatment of 1 with Triethylamine A mixture of **1** (500 mg) and triethylamine (0.5 ml) in acetonitrile (10 ml) was heated at 80 °C for 10 min. The mixture was quenched with 1 N HCl (5 ml) at 0 °C, concentrated to *ca.* 5 ml, and chromatographed over Sephadex LH-20 (3.0 cm i.d. × 35 cm) with 80% aqueous MeOH to yield **5** (53 mg) and **3** (167 mg). **3**: A yellow amorphous powder, $[\alpha]_D^{28}$ −75.1° (c=0.9, MeOH). *Anal.* Calcd for $C_{40}H_{28}O_{25}\cdot 7H_2O$: C, 46.43; H, 4.09. Found: C, 46.67; H, 3.54. Negative FAB-MS m/z: 907 $(M-H)^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz) δ: 2.71 (1H, dd, J=2, 19 Hz, H-5′), 3.12 (1H, dd, J=7, 19 Hz, H-5′), 4.26 (1H, d, J=5 Hz, H-2), 4.42 (1H, dd, J=7, 11 Hz, H-6), 4.61—4.74 (3H, m, H-4′, 5, 6), 4.87 (1H, d, J=4 Hz, H-3), 5.64 (1H, d, J=4 Hz, H-4), 6.23 (1H, d, J=5 Hz, H-1), 6.67, 6.89 (each 1H, s, HHDP H), 7.20 (2H, s, galloyl H), 7.47 (1H, s, H-3″). ^{13}C-NMR (acetone-d_6 + D_2O, 25.05 MHz) δ: 38.0 (C-5′), 41.7 (C-4′), 64.5 (C-6), 65.8 (C-4), 70.7 (C-2), 72.6 (C-3), 74.1 (C-5), 94.3 (C-1), 108.3, 109.6 109.9 (C-3″, HHDP 3, 3′), 110.6 (galloyl 2,6), 115.0 (C-1″), 115.3, 116.0 (HHDP 1,1′), 116.4 (C-2″), 120.5 (galloyl 1), 125.2, 125.5 (HHDP 2,2′), 136.5, 137.2, 138.3, 139.6, 140.4 (C-4″, 5″, galloyl 4, HHDP 5, 5′), 143.6 (C-6″), 144.9, 145.3, 146.0 (galloyl 3, 5, HHDP 4,4′, 6, 6′), 147.8, 149.9 (C-2′, 3′), 161.1 (C-7″), 165.9, 166.8, 168.3 (COO), 172.1 (C-6′), 193.8 (C-1′).

Acid Hydrolysis of 3 **3** (50 mg) was hydrolyzed with 5% HCl at 100 °C for 50 min. The mixture was directly subjected to MCI-gel CHP 20P chromatography (1.0 cm i.d. × 15 cm). Elution with 25% MeOH yielded **4** (7 mg) and **5** (12 mg). **4**: A yellow powder (H_2O–MeOH), mp >300 °C. $[\alpha]_D^{25}$ +29.5° (c=0.3, MeOH). Negative FAB-MS m/z: 291 $(M-H)^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz) δ: 2.58 (1H, d, J=19 Hz, H-5), 3.09 (1H, dd, J=7, 19 Hz, H-5), 4.56 (1H, dd, J=4, 7 Hz, H-4). 7.45 (1H, s, H-3′). ^{13}C-NMR (acetone-d_6 + D_2O, 67.8 MHz) δ: 38.4 (C-5), 42.1 (C-4), 109.4 (C-3′), 114.8 (C-1′), 116.4 (C-2′), 140.0 (C-5′), 140.9 (C-3), 144.3 (C-6′), 147.2 (C-4′), 150.2 (C-2), 161.7 (C-7′), 174.9 (C-6), 194.7 (C-1).

Treatment of 1 with Sodium Benzenesulfinate A mixture of **1** (500 mg) and sodium benzenesulfinate (300 mg) in acetonitrile (10 ml) was heated at 80 °C for 3 h. The reaction mixture was worked up in a manner similar to that described for **3**, and chromatographed on MCI-gel CHP 20P (3.0 cm i.d. × 35 cm). After concentration of the 30% MeOH eluate, the crystalline powder formed was collected by filtration and recrystallized from H_2O to furnish **6** as colorless needles (62 mg), mp 215 °C (dec.). $[\alpha]_D^{28}$ −101.3° (c=0.6, MeOH). *Anal.* Calcd for $C_{40}H_{28}O_{25}\cdot 1/2H_2O$: C, 52.36; H, 3.19. Found: C, 52.10; H, 3.00. Negative FAB-MS m/z: 907 $(M-H)^-$. ^{1}H-NMR (acetone-d_6, 100 MHz) δ: 2.66 (1H, dd, J=6, 17 Hz, H-5′), 2.92 (1H, d, J=17 Hz, H-5′), 3.92 (1H, d, J=4 Hz, H-5), 4.45 (1H, dd, J=4, 11 Hz, H-6), 4.56 (1H, d, J=6 Hz, H-4′), 4.58 (1H, d, J=11 Hz, H-6), 5.12 (1H, d, J=4 Hz, H-4), 5.38 (1H, dd, J=1, 3 Hz, H-2), 5.46 (1H, br d, J=4 Hz, H-3), 6.20 (1H, d, J=3 Hz, H-1), 6.64, 7.03 (each 1H, s, HHDP H), 7.17 (2H, s, galloyl H), 7.23 (1H, s, H-3″). ^{13}C-NMR (acetone-d_6 + D_2O, 25.05 MHz) δ: 38.1 (C-5′), 46.9 (C-4′), 64.3 (C-6), 64.8, 65.8, 71.4, 74.3 (C-2, 3, 4, 5), 91.6 (C-1), 108.2, 110.1 (HHDP 3, 3′), 110.6 (galloyl 2, 6), 111.6 (C-3″), 115.1, 116.6 (C-1″, HHDP 1, 1′), 120.3 (C-2″, galloyl 1), 125.0, 125.5 (HHDP 2, 2′), 136.4, 137.1, 137.5, 138.8, 139.6 (C-3′, 5″, galloyl 4, HHDP 5, 5′), 144.3, 144.7, 144.9, 145.1, 145.3, 145.7 (C-4″, 6″, HHDP 4, 4′, 6, 6′), 146.0 (galloyl 3, 5), 153.0 (C-2′), 164.9, 165.8, 166.1, 168.4, 170.8 (COO), 200.9 (C-1′). The mother liquor was subjected to Bondapak C_{18}/Porasil B chromatography with H_2O–MeOH (1:0—2:3) to give **3** (15 mg). Treatment of **1** (3 g) with sodium benzenesulfinate (2 g) in acetonitrile (50 ml) under reflux for 4 h yielded **5** (212 mg), **6** (135 mg) and **3** (800 mg).

Treatment of 1 with Pyridine A mixture of **1** (2 g) and pyridine (2 ml) in acetonitrile (48 ml) was heated at 80 °C with stirring for 90 min. The reaction mixture was concentrated *in vacuo*, quenched with 1 N HCl (5 ml), and chromatographed over Sephadex LH-20 (3.0 cm i.d. × 40 cm) with 80—100% MeOH to yield **5** (80 mg), **3** (81 mg), **7** (34 mg) and **8** (708 mg). **7**: A tan amorphous powder. $[\alpha]_D^{22}$ +44.8° (c=1.1, MeOH). *Anal.* Calcd for $C_{31}H_{28}O_{26}\cdot 3/2H_2O$: C, 51.10; H, 3.24. Found: C, 50.92; H, 2.84. Negative FAB-MS m/z: 935 $(M-H)^-$. ^{1}H-NMR (acetone-d_6, 100 MHz) δ: 4.00 (1H, dd, J=8, 12 Hz, H-6), 4.63—4.85 (2H, m, H-5, 6), 5.20 (1H, d, J=4 Hz, H-3), 5.46 (1H, d, J=4 Hz, H-4), 5.56 (1H, d, J=6 Hz, H-2), 6.17 (1H, d, J=6 Hz, H-1), 6.65, 7.38, 6.93, 6.94 (each 1H, s, HHDP H), 7.14 (2H, s, galloyl H). **8**: A tan amorphous powder. $[\alpha]_D^{22}$ −20.5° (c=0.6, acetone). *Anal.* Calcd for $C_{41}H_{26}O_{25}\cdot H_2O$: C, 52.57; H, 3.01. Found: C, 52.34; H, 2.79. Negative FAB-MS m/z: 917 $(M-H)^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz) δ: 4.36 (1H, dd, J=6, 12 Hz, H-6), 4.71 (1H, dd, J=8, 12 Hz, H-6), 4.94 (1H, dd, J=6, 8 Hz, H-5), 5.37 (1H, br d, J=4 Hz, H-4), 5.47 (1H, dt, J=1, 4 Hz, H-2), 6.32 (1H, d, J=4 Hz, H-1), 6.69 (1H, dd, J=1, 4 Hz, H-3), 6.74, 7.10, 7.14, 7.37 (each 1H, s, aromatic H), 7.14 (2H, s, galloyl H).

Treatment of 1 with Sodium Hydroxide A solution of **1** (1 g) in 0.2% aqueous NaOH (60 ml) was bubbled with nitrogen gas for 30 min, and heated at 70 °C for 5 min. The mixture was neutralized with 1 N H_2SO_4, and directly subjected to MCI-gel CHP 20P chromatography (3.0 cm i.d. × 30 cm) with H_2O–MeOH (1:0—3:2) to yield **10** (167 mg), **5** (168 mg) and **3** (119 mg). **10**: A white amorphous powder. $[\alpha]_D^{25}$ −54.3° (c=0.9, MeOH). ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz) δ: 4.23 (1H, d, J=4 Hz, H-2), 4.29 (1H, dd, J=8, 11 Hz, H-6), 4.60 (1H, dd, J=7, 8 Hz, H-5), 4.69 (1H, dd, J=7, 11 Hz, H-6), 4.88 (1H, br d, J=3 Hz, H-3), 5.32 (1H, d, J=2 Hz, H-2′), 5.56 (1H, d, J=2 Hz, H-3′), 5.60 (1H, br d, J=3 Hz, H-4), 6.23 (1H, d, J=4 Hz, H-1), 6.70, 6.85 (each 1H, s, HHDP H), 7.13 (2H, s, H-3″, 5′), 7.15 (2H, s, galloyl H).

Treatment of 11 with Triethylamine A mixture of **11** (500 mg) and triethylamine (0.5 ml) in acetonitrile (10 ml) was heated at 80 °C for 7 min. The reaction mixture was worked up in a manner similar to that described for **1** to give **12** (106 mg) as a tan amorphous powder. $[\alpha]_D^{25}$ −166.9° (c=1.0, MeOH). *Anal.* Calcd for $C_{40}H_{28}O_{25}\cdot 3/2H_2O$: C, 51.35; H, 3.34. Found: C, 51.42; H, 3.27. Negative FAB-MS m/z: 907 $(M-H)^-$. ^{1}H-NMR (acetone-d_6, 270 MHz) δ: 2.61 (1H, dd, J=2, 19 Hz, H-5′), 3.04 (1H, dd, J=8, 19 Hz, H-5′), 4.17 (1H, dd, J=5, 8 Hz, H-6), 4.39 (1H, br d, J=3 Hz, H-4), 4.59 (1H, dd, J=5, 8 Hz, H-6), 4.66 (1H, dd, J=5, 8 Hz, H-5), 4.69 (1H, dd, J=2, 8 Hz, H-4′), 4.80 (1H, br s, H-3), 5.19 (1H, br d, J=4 Hz, H-2), 6.46 (1H, d, J=4 Hz, H-1), 6.69, 6.85 (each 1H, s, HHDP H), 7.15 (2H, s, galloyl H), 7.42 (1H, s, H-3″). ^{13}C-NMR (acetone-d_6+D_2O, 25.05 MHz) δ: 37.7 (C-5′), 41.7 (C-4′), 61.1 (C-4), 64.3 (C-6), 71.3, 71.5 (C-2, 3), 76.1 (C-5), 91.4 (C-1), 108.1, 109.5, 109.8 (C-3′, HHDP 3, 3′), 110.5 (galloyl 2, 6), 114.7 (C-1″), 115.9, 116.6 (C-2″, HHDP 1, 1′), 120.0 (galloyl 1), 125.1, 125.3 (HHDP 2, 2′), 136.7, 137.1, 138.7, 139.8, 140.7 (C-4″, 5″, galloyl 4, HHDP 5, 5′), 143.6 (C-6″), 144.8, 145.3, 146.0 (galloyl 3, 5, HHDP 4, 4′, 6, 6′), 147.5, 150.2 (C-2′, 3′), 161.4 (C-7″), 165.6, 167.2, 168.5 (COO), 172.4 (C-6′), 193.9 (C-1′). Acid hydrolysis of **12** (30 mg) in a manner similar to that described for **3**, yielded **4** (5 mg) ($[\alpha]_D^{24}$ −8.4° (c=0.5, MeOH)) and **5** (9 mg).

Treatment of 13 with Triethylamine A mixture of **13** (300 mg) and triethylamine (0.5 ml) in acetonitrile (10 ml) was heated at 80 °C for 7 min. The reaction mixture was worked up in a manner similar to that described for **1** to yield **15** (45 mg) as a tan amorphpous powder. $[\alpha]_D^{28}$ −1.8° (c=0.5, MeOH). *Anal.* Calcd for $C_{33}H_{24}O_{21}\cdot 2H_2O$: C, 50.01; H, 3.56. Found: C, 50.19; H, 3.45. Negative FAB-MS m/z: 756 (M^-). ^{1}H-NMR (acetone-d_6+D_2O, 270 MHz) δ: 2.64 (1H, dd, J=2, 19 Hz, H-5′), 3.07 (1H, dd, J=8, 19 Hz, H-5′), 3.91 (1H, t, J=6 Hz, H-3), 4.03—4.19 (2H, m, H-5, 6), 4.56 (1H, t, J=10 Hz, H-6), 4.69 (1H, dd, J=2, 8 Hz, H-4′), 5.01 (1H, dd, J=2, 6 Hz, H-2), 5.94 (1H, d, J=2 Hz, H-1), 6.80, 6.81 (each 1H, s, HHDP H), 7.41 (1H, s, H-3″). ^{13}C-NMR (acetone-d_6+D_2O, 25.05 MHz) δ: 38.1 (C-5′), 41.7 (C-4′), 65.2, 69.7, 70.8, 74.5, 76.1 (C-2, 3, 4, 5, 6), 93.8 (C-1), 109.0, 109.4 (C-3″, HHDP 3, 3′), 114.1 (C-1″), 115.9, 116.0, 116.7 (C-2″, HHDP 1, 1′), 125.2, 125.6 (HHDP 2, 2′), 136.5, 137.0, 139.2 (C-4″, 5″, HHDP 5, 5′), 141.8 (C-6″), 144.1, 144.8, 145.0 (HHDP 4, 4′, 6, 6′), 147.5, 150.6 (C-2′, 3′), 161.6 (C-7″), 166.7, 169.0 (COO), 173.0 (C-6′), 194.2 (C-1′).

Treatment of 13 with Pyridine A mixture of **13** (300 mg) and pyridine (0.5 ml) in acetonitrile (10 ml) was heated at 80 °C for 1 h. The reaction mixture was worked up in a manner similar to that described for **1**, and chromatographed over Sephadex LH-20 (2.0 cm i.d. × 20 cm) with 80% MeOH to yield **17** (51 mg) as a tan amorphous powder. $[\alpha]_D^{28}$ −68.2° (c=0.5, MeOH). *Anal.* Calcd for $C_{34}H_{22}O_{21}\cdot 5/2H_2O$: C, 50.32; H, 3.35. Found: C, 50.15; H, 3.20. Negative FAB-MS m/z: 765 $(M-H)^-$. ^{1}H-NMR (acetone-d_6, 100 MHz) δ: 4.04 (1H, dd, J=5, 11 Hz, H-6), 4.48 (1H, dd, J=5, 11 Hz, H-5), 4.90 (1H, d, J=2 Hz, H-3), 5.12 (1H, br s, H-2), 5.37 (1H, t, J=11 Hz, H-6), 5.89 (1H, br s, H-4), 5.99 (1H, s, H-1), 6.74, 6.84, 7.07, 7.16 (each 1H, s, aromatic H). ^{13}C-NMR (acetone-d_6, 25.05 MHz) δ: 58.4 64.7, 71.3, 72.3, 72.5 (C-2, 3, 4, 5, 6), 91.1 (C-1), 108.7, 109.8 (HHDP 3, 3′), 112.7, 113.8 [dibenzofurandicarboxyl (DB) 3, 3′], 114.9, 115.2, 115.5, 116.8 (DB 1, 1′, HHDP 1, 1′), 118.6, 119.6 (DB 2, 2′), 126.0 (HHDP 2, 2′), 133.6, 134.1 (DB 5, 5′), 136.2, 136.9 (HHDP 5, 5′), 144.6, 144.7, 145.0, 147.0 (DB 4, 4′, 6, 6′, HHDP 4, 4′, 6, 6′), 166.2, 168.5, 169.2 (COO).

Treatment of 2 with Pyridine A mixture of **2** (1 g) and pyridine (1.5 ml) in acetonitrile (40 ml) was heated at 80 °C with stirring for 90 min. The resulting mixture was worked up as described for **1**, yielding **9** (275 mg) as a tan amorphous powder. $[\alpha]_D^{28}$ +11.5° (c=1.0, MeOH). *Anal.* Calcd for $C_{48}H_{30}O_{30}\cdot 4H_2O$: C, 49.75; H, 3.30. Found: C, 50.13; H, 3.05. Negative FAB-MS m/z: 1085 $(M-H)^-$. ^{1}H-NMR (acetone-d_6, 100 MHz) δ: 4.19 (1H, d, J=11 Hz, H-6), 4.75 (2H, m, H-5, 6), 5.14 (1H, dt, J=1, 5 Hz, H-2), 5.29 (1H, d, J=3 Hz, H-4), 6.27 (1H, d, J=5 Hz, H-1), 6.58 (1H, dd, J=1, 3 Hz, H-3), 6.71, 6.80, 7.09, 7.27, 7.31 (each 1H, s, aromatic H), 7.18 (2H, s, galloyl H). ^{13}C-NMR (acetone-d_6, 25.05 MHz) δ: 64.2 (C-4), 65.3 (C-6), 69.0 (C-2), 75.4 (C-3), 76.8 (C-5), 91.8 (C-1), 108.1, 108.6, 110.1 (valoneayl 3, 3′, 3″), 110.7, 111.1 (DB 3, 3′, galloyl 2, 6), 115.4, 115.7, 116.1, 116.5 (DB 1, 1′, valoneayl 1, 2″), 118.6 (valoneayl 1′), 119.9, 120.2 (DB 2, 2′, galloyl 1), 124.7, 124.8 (valoneayl 2, 2′), 133.3, 135.9 (DB 5, 5′), 136.4, 138.1, 138.5, 139.9, 140.5 (galloyl 4, valoneayl 4″, 5, 5′, 5″, 6″), 143.0 (valoneayl 1″), 144.6, 145.0, 145.2, 145.7, 145.8 (DB 4, 4′, 6, 6′, galloyl 3, 5, valoneayl 4, 6, 6′), 147.0 (valoneayl 4′), 165.0, 166.3, 166.9, 167.6, 168.7, 169.1 (COO).

Treatment of 14 with Triethylamine A mixture of **14** (300 mg) and triethylamine (0.5 ml) in acetonitrile (7 ml) was heated under reflux for 10 min. The reaction mixture was worked up in a manner similar to that described for **1** to give **16** (67 mg) as a pale yellow amorphous powder. $[\alpha]_D^{25}$ +48.6° (c=0.6, acetone). *Anal.* Calcd for $C_{40}H_{28}O_{25}\cdot H_2O$: C, 51.85; H, 3.26. Found: C, 51.84; H, 3.15. Negative FAB-MS m/z: 907 $(M-H)^-$, ^{1}H-NMR (acetone-d_6, 270 MHz) δ: 2.44 (1H, dd, J=3, 19 Hz, H-5′), 3.12 (1H, dd, J=7, 19 Hz, H-5′), 4.12 (1H, t, J=6 Hz, H-4), 4.57 (1H, dd, J=3, 7 Hz, H-4′), 5.12 (1H, dd, J=2, 6 Hz, H-2), 5.20 (1H, dd, J=4, 6 Hz, H-3), 5.83 (1H, d, J=2 Hz, H-1), 6.86, 6.94 (each 1H, s, HHDP H), 7.18 (2H, s, galloyl H), 7.43 (1H, s, H-3′).

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