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BISCHOFIANIN, A DIMERIC DEHYDROELLAGITANNIN FROM *BISCHOFIA JAVANICA*

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Key Word Index—*Bischofia javanica*; Euphorbiaceae; leaves; tannin; dimeric dehydroellagitannin; bischofianin.

Abstract—A new dimeric ellagitannin, bischofianin, was isolated from the leaves of *Bischofia javanica*, together with five known tannins. The structure was elucidated on the basis of spectroscopic and chemical evidence.

INTRODUCTION

Bischofia javanica is a common subtropical tree and cultivated as an avenue tree. The leaves and bark are known to be rich in tannins. In continuing systematic chemical studies on tannins of euphorbiaceous plants [1–4], we have now examined the leaves of this species and isolated a new dimeric ellagitannin, bischofianin, which consists of galloylglucose and dehydroellagitannin moieties. This paper deals with the isolation and structural elucidation of this tannin.

RESULTS AND DISCUSSION

The dried leaves of *B. javanica* were extracted with aqueous acetone and the extract was separated by a combination of chromatography on Sephadex LH-20, cellulose and various reverse-phase gels, such as MCI-gel CHP 20P and Bondapak C_{18}/Porasil B, to yield bischofianin (**1**), together with five known tannins, geraniin (**2**) [5], corilagin (**3**) [6], furosin (**4**) [7], punicalagin (**5**) [8] and procyanidin B-1 (**6**) [9], which were identified by comparison of their physical and spectral data with those described in the literature or by direct comparison with authentic samples.

Bischofianin (**1**) was characterized as an ellagitannin by its blue coloration with $FeCl_3$ reagent and reddish-brown coloration with $NaNO_2$–acetic acid [10]. The ^{13}C NMR spectrum showed signals owing to a cyclohexenetrione ring of a dehydrohexahydroxydiphenoyl (DHHDP) group [δ45.9, 51.9 (CH); 92.1, 93.8, 96.2, 108.9 (hemiketal); 125.4, 128.9, 148.8, 154.1 (olefin); 192.1, 195.0 (ketone)], the chemical shifts of which were closely related to those of geraniin (**2**). Because of the equilibrium between five-and six- membered hemiketal ring structures of the DHHDP group, the ^1H and ^{13}C NMR spectra were complicated, hence **1** was treated with *o*-phenylenediamine to give the phenazine derivative, **1a**. The ^1H NMR spectrum of **1a** showed five two-proton aromatic singlets (δ6.98, 7.08, 7.10, 7.13, 7.16) attributable to five galloyl groups, and two anomeric doublets at δ5.95 (J = 8 Hz) and 6.21 (J = 6 Hz) indicating the presence of two sugar residues. The dimeric structure of **1** was further supported by the negative FAB-mass spectra of **1** and **1a** which showed $[M - H]^-$ peaks at m/z 1871 and 1943, respectively.

Partial hydrolysis of **1a** in hot water afforded three major products, phenazine bislactone (**1b**) [5], 1,2,3,6-tetra-*O*-galloyl-β-D-glucopyranose (**1c**) [11] and phillyl-aeoidin E (**1d**) [12], suggesting that the valoneyl ester group attached to the C-4 hydroxyl group of **1d** links the two sugar moieties together in the molecule of **1**. To determine the location of the esters in the other unit, we applied the reaction of dehydroellagitannins with L-cysteine methyl ester [13] for selective hydrolysis of the DHHDP group to yield **1e** and **f**. The ^1H NMR spectrum of **1e** showed signals due to two sugar moieties (see Experimental), the chemical shifts and coupling constants of which were almost in line with those of corilagin (**3**) plus pentagalloylglucose, except for the large upfield shifts of H-5 [δ3.51 (*d*, J = 10 Hz)] and one of the H-6 [δ3.67 (*d*, J = 12 Hz)] of the pentagalloylglucose moiety [pentagalloylglucose: δ4.61 (H-5), 4.50 (2H, H-6)] [14]. These upfield shifts were considered to be caused by the anisotropic effect of the corilagin moiety. The ^1H–^{13}C long-range COSY spectrum of **1e** showed correlation peaks between the aromatic singlet attributable to the H-3′ of the valoneyl group (δ6.26) [7, 15] and the carboxyl carbon (C-7′) signal at δ168.4, which was also correlated to the signal owing to glucose H-6 (δ4.70) of the corilagin

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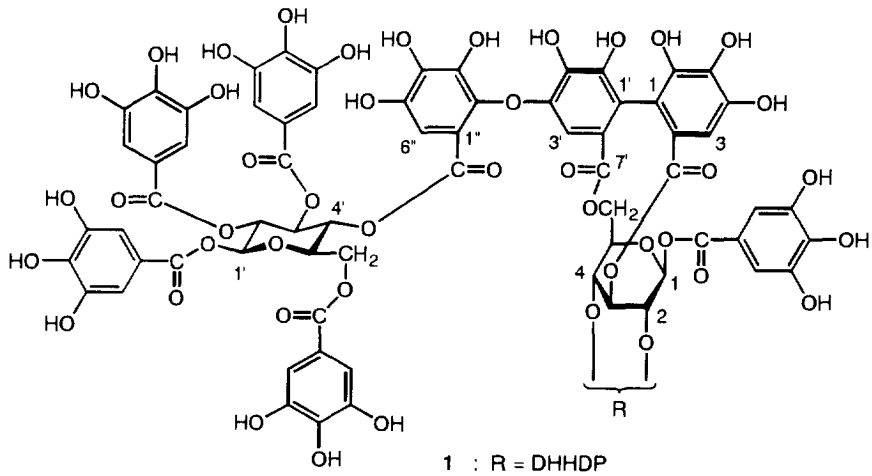
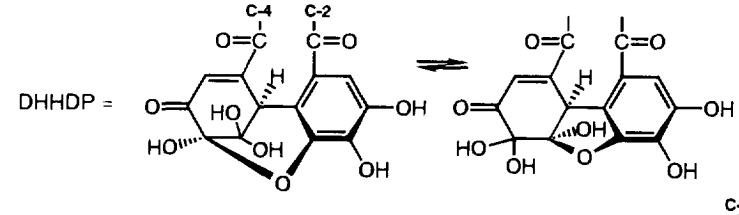
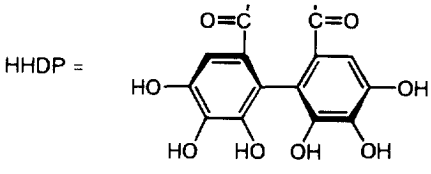
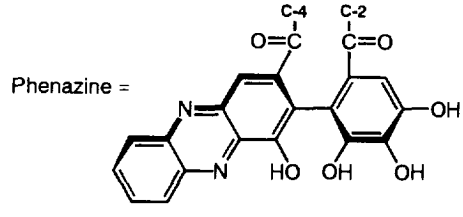


1 : R = DHHDP
1a : R = Phenazine
1e : R = H, H
1g : R = HHDP







moiety. These results indicated that the structure of **1e**, including the orientation of the valoneyl group, was represented by the formula **1e**.

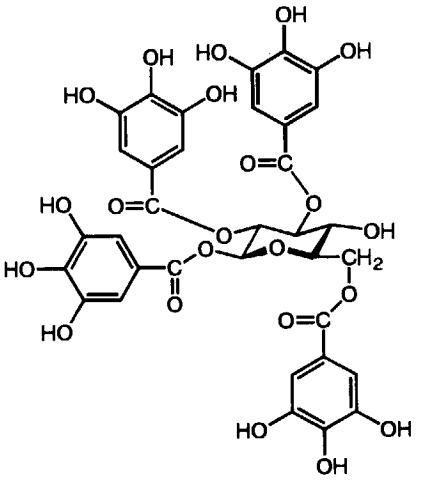
The orientation of the DHHDP group attached to C-2 and C-4 hydroxyl group of the glucose was determined to be the same as that of geraniin (**2**), on the basis of the upfield shift of the anomeric proton signal (δ6.21) in **1a** as compared with that of **1** (δ6.64 and 6.60). This phenomenon was similarly observed in the case of **2** and its phenazine derivative [5]. The configuration of the DHHDP and valoneyl groups were determined to be *R* by methylation followed by methanolysis of **1g**, which was prepared by catalytic reduction of **1**, to yield methyl trimethoxybenzoate, dimethyl (*R*)-4,4',5,5',6,6'-hexamethoxydiphenate [5] and trimethyl (*R*)-octamethylvaloneate [16]. On the basis of these results, the structure of bischofianin was concluded to be that represented by formula **1**. This tannin is considered to be biosynthesized by oxidative coupling between geraniin (**2**) and pentagalloylglucose. Although **2** is the major constituent of the leaves (1.8% dry weight), pentagalloylglucose was not detected.

EXPERIMENTAL

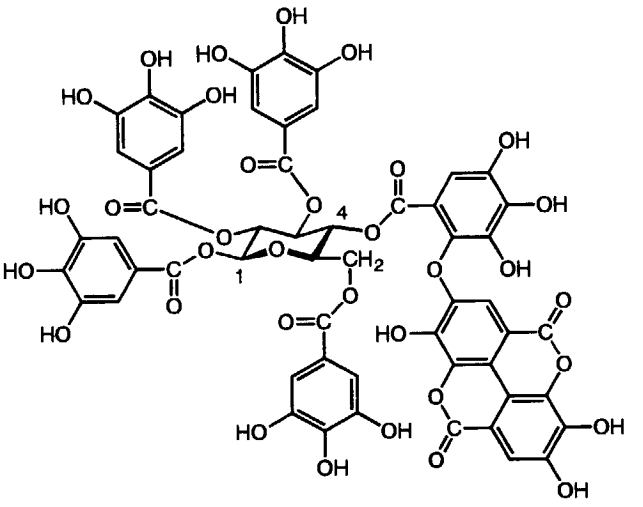
General. NMR spectra were recorded at 100 and 270 MHz (^{1}H NMR) and 25 MHz (^{13}C NMR). Chemical shifts are given in δ (ppm) with TMS as int. std. Negative FAB-MS were measured at 1.5 kV (accelerating voltage) with MeOH–glycerol as matrix. CC was carried out on Sephadex LH-20 (25-100 μm, Pharmacia), MCI gel CHP 20P (75–150 μm, Mitsubishi), Bondapak C_{18}/Porasil B (37–75 μm, Waters), Avicel cellulose (Funakoshi), Cosmosil 75C_{18}-OPN (75 μm, Nacalai Tesque) and Kieselgel 60 (70–230 mesh, Merck). TLC was conducted on precoated silica gel 60 F_{254} plates (Merck) and precoated cellulose F_{254} plates (Merck). Spots were detected under UV and by spraying with ethanolic $FeCl_3$.

Plant material. Leaves of *B. javanica* Bl. were collected in the Taiwan Forestry Research Institute, Heng-chun Branch, Taiwan, R.O.C.

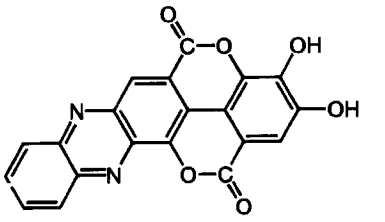
Extraction and isolation. Dried leaves (2.8 kg) were extracted with Me_2CO–H_2O (4:1) at room temp. After removal of Me_2CO *in vacuo*, the aq. soln was filtered and the filtrate subjected to Sephadex LH-20 CC with H_2O



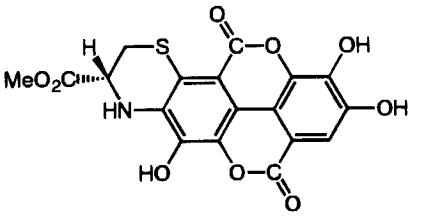
1c



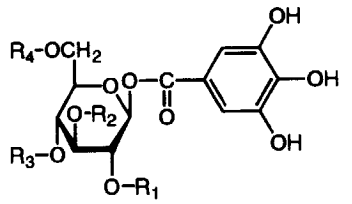
1d



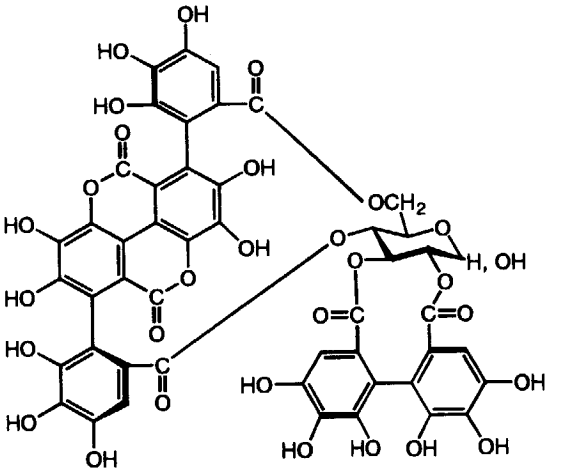
1b



1f



2: R_1-R_3 = DHHDP; R_2-R_4 = HHDP
3: R_1=R_3=H; R_2-R_4 = HHDP
4: R_1-R_3 = DHHDP; R_2-R_4 =H



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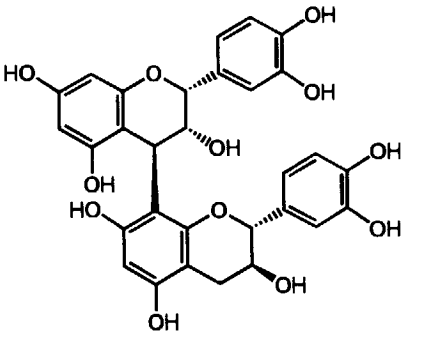

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containing increasing proportions of MeOH, and finally with 50% aq. Me_2CO, to yield four frs, I (50 g), II (19 g), III (57 g) and IV (28 g). Fr. II was sepd by a combination of CC over Sephadex LH-20 (EtOH), MCI-gel CHP 20P (H_2O–MeOH) and Avicel cellulose (2% HOAc) to afford corilagin (**3**) (2.2 g), furosin (**4**) (1.1 g) and procyanidin B-1 (**6**) (41 mg). Repeated CC of fr. III over Sephadex LH-20 (60% MeOH) and MCI-gel CHP 20P (35% MeOH) yielded geraniin (**2**) (50 g) and punicalagin (**5**) (72 mg). Fr. IV was applied to a column of Sephadex LH-20 with MeOH–H_2O–Me_2CO (8:1:1) and then Bondapak C_{18}/Porasil B (20% MeOH) to yield bischofianin (**1**) (2.2 g).

Bischofianin (**1**). Brown amorphous powder. $[\alpha]_D^{24}$ − 20.5° (MeOH; *c* 2.4). Negative FAB-MS *m/z*: 1889 $[M - H]^-$. ^1H NMR (Me_2CO-d_6 + D_2O): δ7.27, 7.26 [1H, in total, each *s*, valoneyl(val)-6″], 7.17, 7.16, 7.15, 7.12, 7.10, 7.06 (11H in total, each *s*, DHHDP-3′, galloyl-H), 6.64, 6.60 (1H, in total, each *s*, Glc-1), 6.57, 6.56 (1H in total, each *s*, Val-3), 6.21 (1H, *s*, Val-3′), 5.98, 5.96 (1H, in total, each *d*, *J* = 8 Hz, Glc-1′), 5.83 (1H, *t*, *J* = 10 Hz, Glc-3′), 5.69 (1H, *t*, *J* = 10 Hz, Glc-4′), 5.43–5.65 (4H, *m*, Glc-2), 2′, 3, 4), 5.22 (2/5H, *s*, DHHDP-1), 4.94 (3/5H, *d*, *J* = 1 Hz, DHHDP-1), 4.79 (2H, *m*, Glc-5, 6) 4.35 (1H, *d*, *J* = 11 Hz, Glc-6′), 3.64–3.85 (Glc-6, 6′, overlapped with HOD signal), 3.45 (1H, *br d*, *J* = 10 Hz, Glc-5′). ^{13}C NMR (Me_2CO-d_6 + D_2O): δ93.8 (C-1′), 74.1 (C-5′), 73.0 (C-3′), 71.4 (C-2′), 68.4 (C-4′), 61.4 (C-6′) (glucose of pentagalloylglucose unit); 92.1, 91.5 (C-1), 73.3, 72.5, 71.0, 70.3, 67.0, 66.0, 64.0, 63.7, 62.8 (C-6) (glucose of geraniin unit); 192.1 (C-4), 154.1 (C-2), 145.0 (C-4′), 143.6 (C-6′), 128.9 (C-3), 115.8 (C-1′), 113.5 (C-3′), 96.2 (C-5), 92.4 (C-6), 45.9 (C-1) (six-membered ring structure of DHHDP); 195.0 (C-4), 148.8 (C-2), 125.4 (C-3), 108.9 (C-6), 92.1 (C-5), 51.9 (C-1) (five-membered ring structure of DHHDP); 103.4 (Val-3′), 106.8 (Val-3), 147.9 (Val-4′); 110.0, 110.2, 110.5 (galloyl-2, 6); 164.6, 165.0, 165.5, 166.0, 166.4, 166.7, 167.0, 168.3 (CO_2). (Found: C, 50.57; H, 3.64. $C_{82}H_{58}O_{53}\cdot 3H_2O$ requires: C, 50.62; H, 3.32).

Phenazine derivative (**1a**). A mixt. of **1** (100 mg) and *o*-phenylenediamine (8 mg) in 20% HOAc–EtOH was left standing for 30 min. The product was purified by Sephadex LH-20 CC with MeOH–H_2O–Me_2CO (14:3:3) to give **1a** (42 mg) as a yellow powder. $[\alpha]_D^{25}$ + 13.3° (MeOH; *c* 0.2). Negative FAB-MS *m/z*: 1943 $[M - H]^-$. ^1H NMR (Me_2CO-d_6 + D_2O): δ8.30–8.37 [2H, *m*, phenazine(phe)-4″, 5″), 8.33 (1H, *s*, phe-3), 8.05 (2H, *m*, phe-3″, 6″) 7.53 (1H, *s*, phe-3′), 7.16, 7.13, 7.10, 7.08, 6.98 (each 2H, *s*, galloyl-H), 7.12 (1H, *s*, Val-3″), 7.07 (1H, *s*, Val-3), 6.26 (1H, *s*, Val-3′), 6.21 (1H, *d*, *J* = 6 Hz, Glc-1), 5.95 (1H, *d*, *J* = 8 Hz, Glc-1′), 5.84 (1H, *t*, *J* = 10 Hz, Glc-3′), 5.74 (1H, *d*, *J* = 6 Hz, Glc-2), 5.73 (1H, *t*, *J* = 10 Hz, Glc-4′), 5.62 (1H, *dd*, *J* = 8, 10 Hz, Glc-2′), 5.57 (1H, *d*, *J* = 5 Hz, Glc-4), 5.42 (1H, *d*, *J* = 4 Hz, Glc-3), 4.97 (1H, *dd*, *J* = 4, 8 Hz, Glc-5), 4.80 (1H, *dd*, *J* = 8, 12 Hz, Glc-6), 4.45 (1H, *d*, *J* = 14 Hz, Glc-6′), 3.88 (1H, *dd*, *J* = 4, 12 Hz, Glc-6), 3.68 (1H, *dd*, *J* = 2, 14 Hz, Glc-6′), 3.47 (1H, *br d*, *J* = 10 Hz, Glc-5′). ^{13}C NMR (Me_2CO-d_6 + D_2O): δ91.7 (C-1), 76.8 (C-5), 76.5 (C-2), 68.6 (C-3), 67.7 (C-4), 65.4 (C-6) (glucose of geraniin unit); 93.7, 74.0, 73.0, 71.4, 68.6, 61.7 (glucose of pentagalloylglucose unit); 164.7, 165.2, 166.0, 166.5, 166.8, 167.0, 168.3 (CO_2). (Found: 52.72; H, 3.27; N, 1.33. $C_{88}H_{60}O_{50}N_2\cdot 3H_2O$ requires: C, 52.86; H, 3.33; N, 1.40).

Partial hydrolysis of compound **1a**. A soln of **1a** (30 mg) in H_2O–MeOH (2:1, 6 ml) was heated at 80° for 27 hr. The resulting red ppts **1b** were collected by filtration. The filtrate was subjected to CC over Sephadex LH-20 (EtOH) and MCI gel CHP 20P (H_2O–MeOH) to afford **1c** (2 mg) and **1d** (5 mg). 1,2,3,6-tetra-*O*-galloyl-β-D-glucose (**1c**). Amorphous powder. $[\alpha]_D^{28}$ + 38.2° (Me_2CO; *c* 0.2). ^1H NMR (Me_2CO-d_6 + D_2O): δ7.17, 7.11, 7.09, 7.03 (each 2H, *s*, galloyl-H), 6.19 (1H, *d*, *J* = 8 Hz, Glc-1), 5.72 (1H, *t*, *J* = 9 Hz, H-3), 5.48 (1H, *t*, *J* = 9 Hz, H-2). Phillylaeoidin E (**1d**). Tan amorphous powder. $[\alpha]_D^{28}$ + 38.1° (Me_2CO; *c* 0.5). ^1H NMR (Me_2CO-d_6 + D_2O): δ7.52, 7.13 (each 1H, *s*, Val-H), 7.04 (2H, *s*, Galloyl-H), 7.01 (3H, *s*, Galloyl-H, Val-H), 6.97, 6.72 (each 2H, *s*, Galloyl-H), 6.21 (1H, *d*, *J* = 8 Hz, Glc-1), 5.94 (1H, *t*, *J* = 10 Hz, Glc-3), 5.72 (1H, *t*, *J* = 10 Hz, Glc-4), 5.55 (1H, *dd*, *J* = 8, 10 Hz, Glc-2), 4.47 (1H, *d*, *J* = 13 Hz, Glc-6), 4.41 (1H, *dd*, *J* = 4, 10 Hz, Glc-5), 3.95 (Glc-6, overlapped with HOD signal).

Partial hydrolysate **1e**. A mixt. of **1** (200 mg), L-cysteine methyl ester (100 mg) and HCO_2NH_4 (50 mg) in H_2O–MeOH (2:1, 20 ml) was heated at 80° for 5 hr. The resulting yellow ppts (**1f**), which were identified by direct comparison of the IR data with an authentic sample, were collected by filtration. CC of the filtrate on Cosmosil 75C_{18}-OPN with 30% MeOH gave hydrolysate **1e** (85 mg) as a tan amorphous powder. $[\alpha]_D^{25}$ − 22.0° (MeOH; *c* 0.5). ^1H NMR (Me_2CO-d_6 + D_2O): δ7.14, 7.12, 7.11, 7.10, 7.06 (each 2H, *s*, galloyl-H), 7.04 (1H, *s*, Val-6″), 6.88 (1H, *s*, Val-3), 6.26 (each 1H, *s*, Val-3′), 6.37 (1H, *d*, *J* = 3 Hz, Glc-1), 6.02 (1H, *d*, *J* = 8 Hz, Glc-1′), 5.83 (1H, *t*, *J* = 10 Hz, Glc-3′), 5.70 (1H, *t*, *J* = 10 Hz, Glc-4′), 5.62 (1H, *dd*, *J* = 8, 10 Hz, Glc-2′), 4.90 (1H, *br s*, Glc-3), 4.70 (1H, *t*, *J* = 10 Hz, Glc-6), 4.50 (2H, *m*, Glc-4, 5), 4.35 (1H, *d*, *J* = 12 Hz, Glc-6′), 4.15 (2H, *m*, Glc-2, 6), 3.67 (1H, *d*, *J* = 12 Hz, Glc-6′), 3.51 (1H, *d*, *J* = 10 Hz, Glc-5′). ^{13}C NMR (Me_2CO-d_6 + D_2O): δ61.3 (Glc-6′), 62.1 (Glc-4), 64.4 (Glc-6), 68.4, 68.8 (Glc-2, 4′), 70.3, 71.1 (Glc-2′, 3), 73.1 (Glc-3′), 74.3 (Glc-5′), 75.5 (Glc-5), 93.9 (Glc-1′), 94.3 (Glc-1), 103.3 (Val-3′), 109.2 (Val-3), 110.0, 110.2, 110.6, 110.8 (Val-6″, Galloyl-2, 6), 113.7 (Val-1″), 116.0 (Val-1), 118.6 (Val-1′), 119.5, 120.0, 120.3, 120.6, 121.6 (galloyl-1), 125.3, 125.7 (Val-2, 2′), 135.5 (Val-3″), 136.2 (Val-5′), 136.5 (Val-5), 139.3 (Val-4″), 138.7, 139.1, 139.5, 140.1, 140.3 (Galloyl-4), 140.6 (Val-5″), 143.6 (Val-2″), 145.0 (Val-4), 145.8, 146.0 (Val-6, 6′, Galloyl-3, 5), 148.1 (Val-4′), 164.1 (Val-7″), 165.1 (2C), 165.9 (2C), 167.0 (galloyl-7), 167.4 (Val-7), 168.4 (Val-7′).

Reduction of compound **1**. A soln of **1** (300 mg) in EtOH (10 ml) was hydrogenated for 10 hr at 25° at atmos. pres. in the presence of 8% Pd-C. After filtration, the product was purified by CC on Sephadex LH-20 (EtOH–H_2O–Me_2CO, 27:18:5) to give **1g** (46 mg) as a tan amorphous powder. $[\alpha]_D^{28}$ + 18.8° (MeOH; *c* 0.5). ^1H NMR (Me_2CO-d_6 + D_2O): δ7.43 (1H, *s*, Val-H), 7.15 (2H, *s*, Galloyl-H), 7.14 (3H, *s*, Val-,H Galloyl-H), 7.13,

7.09, 7.07 (each 2H, *s*, Galloyl-H), 7.05, 6.99 (each 1H, *s*, hexahydroxydiphenoyl-H), 6.21 (1H, *s*, Val-H), 6.16 (1H, *d*, $J = 6$ Hz, Glc-1), 5.93 (1H, *d*, $J = 8$ Hz, Glc-1'), 5.82 (1H, *t*, $J = 10$ Hz, Glc-3'), 5.71 (1H, *t*, $J = 10$ Hz, Glc-4'), 5.65 (1H, *d*, $J = 6$ Hz, Glc-2), 5.61 (1H, *dd*, $J = 8$, 10 Hz, Glc-2'), 5.52 (1H, *d*, $J = 4$ Hz, Glc-4), 5.17 (1H, *d*, $J = 4$ Hz, Glc-3), 4.83 (1H, *dd*, $J = 4$, 8 Hz, Glc-5), 4.74 (1H, *dd*, $J = 8$, 12 Hz, Glc-6), 4.42 (1H, *d*, $J = 12$ Hz, Glc-6'), 3.83 (1H, *dd*, $J = 4$, 12 Hz, Glc-6), 3.66 (1H, *d*, $J = 12$ Hz, H-6'), 3.43 (1H, *d*, $J = 10$ Hz, H-5'). (Found: C, 49.56; H, 3.48. $C_{82}H_{58}O_{52}\cdot 6H_2O$ requires: C, 49.66; H, 3.56).

Methylation followed by methanolysis of compound **1g**. A mixt. of **1g** (40 mg), Me_2SO_4 (1 ml) and K_2CO_3 (2 g) in dry Me_2CO (20 ml) was heated under reflux for 2 hr with stirring. After removal of inorganic material by filtration, the filtrate was concd and subjected to CC on silica gel (C_6H_6–Me_2CO, 9:1). The product (26 mg) was hydrolysed with 5% NaOH in H_2O–MeOH (1:1) (90°, 1 hr). After cooling, the mixt. was acidified with HCl, extracted with Et_2O, dried over Na_2SO_4 and methylated with CH_2N_2. The mixt was sepd by CC on silica gel (C_6H_6–Me_2CO) to yield methyl 3,4,5-trimethoxybenzoate (10 mg), dimethyl(*R*)-4,4',5,5',6,6'-hexamethoxydiphenate (2.7 mg, $[\alpha]_D^{20} + 24.8°$ ($CHCl_3$; *c* 0.3)) and trimethyl(*R*)-octamethylvaloneate (7.2 mg, $[\alpha]_D^{20} + 15.3°$ ($CHCl_3$; *c* 0.7)).

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REFERENCES

1. Lee, S.-H., Tanaka, T., Nonaka, G. and Nishioka, I. (1991) *Chem. Pharm. Bull.* **39**, 630.
2. Lin, J.-H., Tanaka, T., Nonaka, G., Nishioka, I. and Chen, I.-S. (1990) *Chem. Pharm. Bull.* **38**, 2162.
3. Lin, J.-H., Ishimatsu, M., Tanaka, T., Nonaka, G. and Nishioka, I. (1990) *Chem. Pharm. Bull.* **38**, 1844.
4. Nonaka, G., Hayashi, M., Tanaka, T., Saijo, R. and Nishioka, I. (1990) *Chem. Pharm. Bull.* **38**, 861.
5. Okuda, T., Yoshida, T. and Hatano, T. (1982) *J. Chem. Soc. Perkin Trans. I* 9.
6. Tanaka, T., Nonaka, G. and Nishioka, I. (1985) *Phytochemistry* **24**, 2075.
7. Saijo, R., Nonaka, G. and Nishioka, I. (1989) *Chem. Pharm. Bull.* **37**, 2063.
8. Tanaka, T. Nonaka, G. and Nishioka, I. (1986) *Chem. Pharm. Bull.* **34**, 650.
9. Weinges, K., Goritz, K. and Nader, F. (1968) *Liebigs Ann. Chem.* **715**, 168.
10. Bate-Smith, E. C. (1972) *Phytochemistry* **11**, 1153.
11. Nishizawa, M., Yamagishi, T., Nonaka, G. and Nishioka, I. (1983) *J. Chem. Soc. Perkin Trans. I* 961.
12. Nonaka, G., Nakayama, S. and Nishioka, I. (1989) *Chem. Pharm. Bull.* **37**, 2030.
13. Tanaka, T., Fujisaki, H., Nonaka, G. and Nishioka I. (1992) *Heterocycles* **33**, 375.
14. Nishizawa, M., Yamagishi, T., Nonaka, G. and Nishioka, I., (1982) *J. Chem. Soc. Perkin Trans. I* 2963.
15. Xu, Y.-M., Sakai, T., Tanaka, T., Nonaka, G. and Nishioka, I., (1991) *Chem. Pharm. Bull.* **39**, 639.
16. Saijo, R., Nonaka, G., Nishioka, I., Chen, I.-S. and Hwang, T.-H. (1989) *Chem. Pharm. Bull.* **37**, 2940.