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SEDOHEPTULOSE DIGALLATE FROM *CORNUS OFFICINALIS**

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Key Word Index—*Cornus officinalis*; Cornaceae; 1,7-di-*O*-galloyl-D-sedoheptulose; D-sedoheptulose; gallotannin; tannin.

Abstract—A chemical investigation of the leaves of *Cornus officinalis* has led to the isolation and characterization of a novel gallotannin, 1,7-di-*O*-galloyl-D-sedoheptulose, in addition to six galloylglucoses and five ellagitannins. The structure of the new compound was established on the basis of spectroscopic and chemical evidence. This is the first gallotannin possessing a heptose core.

INTRODUCTION

It is well known that sedoheptulose (D-*altro*-heptose) plays important roles in the primary and secondary metabolism of plants, i.e. in the pentose phosphate pathway, the synthesis of carbohydrates during photosynthesis and the biosynthesis of shikimic acid. In the course of a chemical investigation on tannins, we have isolated 1,7,-di-*O*-galloyl-D-sedoheptulose (**1**) from the leaves of *Cornus officinalis* (Cornaceae). This paper deals with the isolation and the structure determination of compound **1**.

RESULTS AND DISCUSSION

The aqueous acetone extract of the fresh leaves of *Cornus officinalis* was subjected to a combination of Sephadex LH-20 and various reversed-phase (MCI-gel CHP 20P, Fuji-gel ODS G3 and Bondapak C_{18}/Porasil B) chromatographies to afford compounds **1**–**12**. Compounds **2**–**12** were identified as 2,3-di-*O*-galloyl-D-glucopyranose (**2**) [2], 1,2-di-*O*-galloyl-β-D-glucopyranose (**3**) [3], 3,4,6-tri-*O*-galloyl-D-glucopyranose (**4**) [Lin, T. C. *et al.*, unpublished data], 1,2,6-tri-*O*-galloyl-β-D-glucopyranose, (**5**) [4], 1,2,4,6-tetra-*O*-galloyl-β-D-glucopyranose (**6**) [5], 1,2,3,6-tetra-*O*-galloyl-β-D-glucopyranose (**7**) [6], 3-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucose (**8**) [7], 2-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucose (**9**) [8], 1-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-α-D-glucose (**10**) [Nonaka, G. *et al*, unpublished data], 1-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-β-D-glucose (**11**) [9], and coriarin F (**12**) [10] by comparisons of the spectroscopic and physical data with those of authentic samples or values reported in the literature.

Compound **1** was obtained as a light tan amorphous powder, $C_{21}H_{22}O_{15} \cdot 2H_2O$ $[\alpha]_D^{20} + 0.4°$ (acetone). A dark blue coloration with the ferric chloride reagent and the appearance of aromatic singlet signals at δ7.16, 7.17 and 7.18 (4H in total) in the ^{1}H NMR spectrum suggested the presence of galloyl groups in the molecule. The ^{13}C NMR spectrum showed, along with signals arising from the galloyl groups, four hemiketal carbon signals (δ105.9, 102.0, 98.3 and 95.6) and complicated oxygen-bearing methine and methylene signals (from δ64.7 to 85.6), suggesting the presence of a carbohydrate moiety. The negative FABMS of **1** exhibited the intense $[M - H]^-$ ion peak at m/z 513, which corresponds to the molecule consisting of two galloyl groups and one heptose moiety. Acid hydrolysis with dilute sulphuric acid yielded gallic acid and a hydrolysate, which was identified as 2,7-anhydro-sedoheptulose (**1a**) by GC of the TMS derivative and co-TLC with an authentic sample. These findings indicated that compound **1** is an equilibrium mixture (α- and β-furanoses and α- and β-pyranoses) of a digalloyl-D-sedoheptulose. Partial hydrolysis of **1** with dilute hydrochloric acid afforded gallic acid and a hydrolysate (**1b**), $C_{14}H_{16}O_{10} \cdot 3H_2O$. The negative FABMS of **1b** showed the $[M - H]^-$ ion peak at m/z 343, suggesting that **1b** is a monogallate of anhydrosedoheptulose. The ^{1}H NMR spectrum was consistent with this mass spectral observation, and fairly lowfield shifts of a pair of geminally coupled doublets (δ4.54 and 4.34, each *d*, $J = 11.9$ Hz) indicated that the galloyl group is attached to the C-1 position. The location of the other galloyl group was determined as follows. Treatment of **1** with phenylhydrazine in the presence of sodium acetate gave the osazone derivative (**1c**), $C_{26}H_{28}O_9N_4 \cdot 3/2H_2O$. The positive FABMS data [m/z 541 $(M + H)^+$] and the ^{1}H NMR two-proton singlet resonance at δ7.00 indicated that **1c** has one galloyl group. Furthermore, the ^{1}H NMR spectrum showed four doublets due to hydroxyl protons [δ5.19 ($J = 5.1$ Hz), 5.02 ($J = 5.3$ Hz), 4.95 ($J = 5.9$ Hz), and 4.85 ($J = 6.6$ Hz)] which are coupled with the C-3, C-6, C-5 and C-4 methine protons, respectively, indicating that the galloyl group is absent at these positions. The signals due to the C-7 methylene protons appeared at relatively lowfield [δ4.33 (*dd*, $J = 2.4$ and 11.4 Hz) and δ4.23 (*dd*, $J = 7.6$ and 11.4 Hz)]. These facts indicated that the galloyl group is attached to the C-7 hydroxyl group and therefore the structure of **1** was characterized as 1,7-di-*O*-galloyl-D-sedoheptulose (**1**). In the plant kingdom, D-glucose is the dominant polyalcohol core of hydrolysable tannins [5], and in some cases, quinic acid [11],

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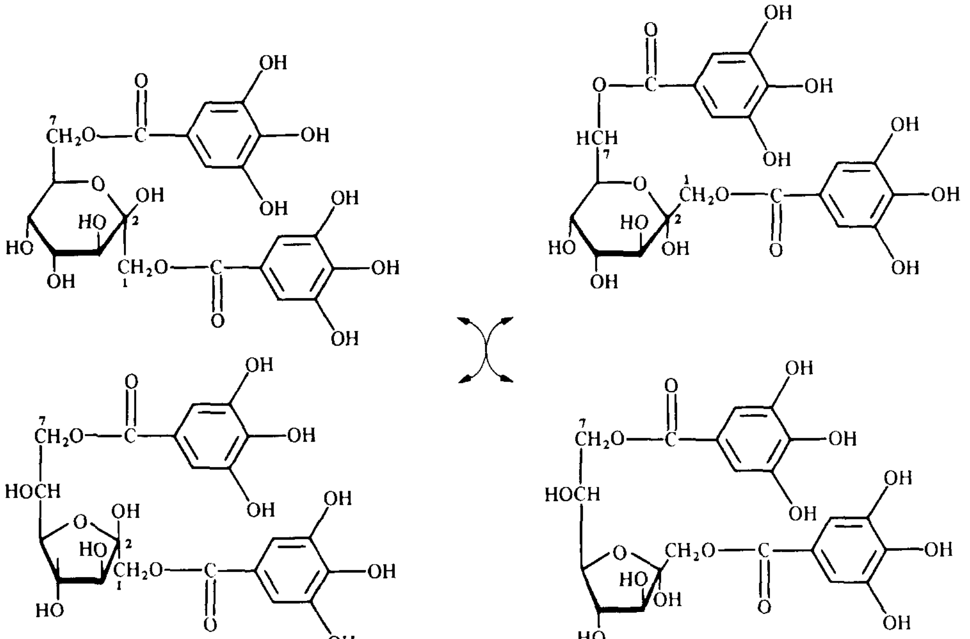
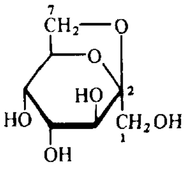
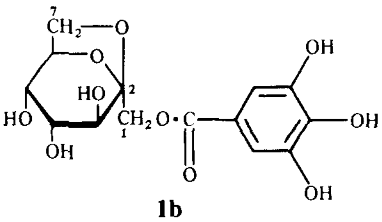
*Part 86 in the series 'Tannins and Related Compounds'. For Part 85 see ref. [1].



1



1a



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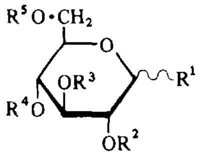
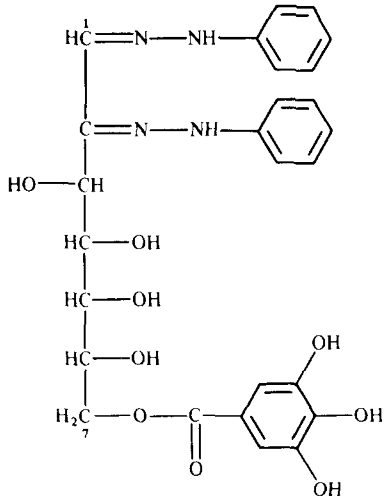
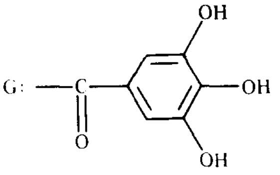


	R^1	R^2	R^3	R^4	R^5
2	OH	G	G	H	H
3	OG	G	H	H	H
4	OH	H	G	G	G
5	(β) OG	G	H	H	G
6	(β) OG	G	H	G	G
7	(β) OG	G	G	H	G



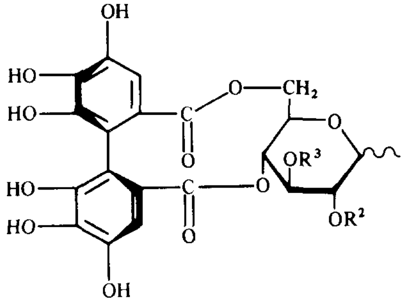
1c



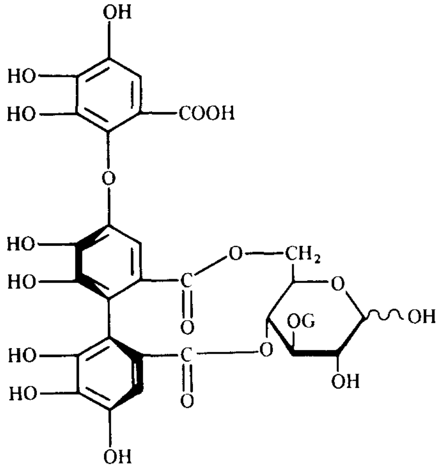
shikimic acid [12], quercitols [13], glucosides [14], 1,5-anhydroglucitol [15], hamamelose [16], etc. are found. Compound **1** is the first gallotannin possessing a heptose core.

EXPERIMENTAL

General. Mps: uncorr. ^1H and ^{13}CNMR spectra were recorded at 270 and 100 MHz (for ^1H) and 25.05 MHz (for ^{13}C) and chemical shifts are given in δ(ppm) scale with TMS as int. standard. FABMS were measured at 2 kV (accelerating voltage) with DMSO-glycerol as matrix. CC was carried out with Sephadex LH-20 (25–100 μ, Pharmacia Fine Chemical Co., Ltd), MCI-gel CHP 20P (75–150 μ, Mitsubishi Chemical Industry Co., Ltd.), Fuji-gel ODS G3 (43–65 μ, Fujigel Hanbai Co., Ltd), and Bondapak C_{18}/Porasil B (37–75 μ, Water Associates Inc.). TLC was conducted on precoated silica gel 60 F_{254} plates (Merck) and precoated cellulose F_{254} plates. Spots were visu-

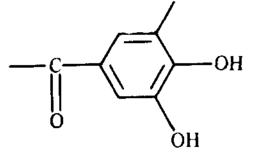


	R¹	R²	R³
8	OH	H	G
9	OH	G	H
10 (α)	OG	H	H
11 (β)	OG	H	H



12

G:



alized under UV and by spraying $FeCl_3$ (for phenolics), and dil. H_2SO_4 (for phenolics and sugars). GC was conducted with N_2 as carrier gas, over 5% SE-30.

Plant material. The leaves of *Cornus officinalis* were collected at the medicinal plant garden in the Kyushu University. A voucher specimen is deposited at the Herbarium, Faculty of Pharmaceutical Sciences, Kyushu University.

Extraction and isolation. Fresh leaves (7 kg) were extracted with 80% aq. Me_2CO at room temp. After removal of Me_2CO *in vacuo*, the insolubles (chlorophylls, etc.) were removed by filtration. The filtrate was concd and then subjected to a column of Sephadex LH-20. Elution with a solvent system of H_2O containing increasing proportion of MeOH afforded four fractions; I (38.6 g), II (71.5 g), III (79.2 g) and IV (66.0 g). Repeated CC of fr. II on MCI-gel CHP 20P, Fuji-gel ODS G3 and Bondapak C_{18}/Porasil B with and H_2O–MeOH gradient solvent system gave 1,7-di-*O*-galloyl-D-sedoheptulose (**1**) (1.4 g), 2,3-di-*O*-galloyl-D-glucopyranose (**2**) (450 mg), 1,2-di-*O*-galloyl-β-D-glucopyranose (**3**) (35 mg), 3,4,6-tri-*O*-galloyl-D-glucopyranose (**4**) (46 mg), 1,2,6-tri-*O*-galloyl-β-D-glucopyranose (**5**) (600 mg), 1,2,4,6-tetra-*O*-galloyl-β-D-glucopyranose (**6**) (27 mg), 1,2,3,6-tetra-*O*-galloyl-β-D-glucopyranose (**7**) (16 mg), 3-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucose (**8**) (110 mg) and 2-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-D-glucose (**9**) (120 mg). Separation of fr. III by repeated CC on Sephadex LH-20 with MeOH, Fuji-gel and Bondapak with H_2O–MeOH (3:1) yielded 1-*O*-galloyl-4,6-(*S*)-hexahydroxy diphenoyl-α-D-glucopyranose (**10**) (210 mg), 1-*O*-galloyl-4,6-(*S*)-hexahydroxydiphenoyl-β-D-glucose (**11**) (870 mg), and coriarin F (12) (136 mg).

1,7-*Di*-O-*galloyl*-D-*sedoheptulose* (**1**). A light tan amorphous powder, $[\alpha]_D^{20}$ +0.4° (MeOH; *c* 0.8). Negative FABMS *m/z*: 513 $[M-H]^-$. ^1H NMR (Me_2CO-d_6 + D_2O): δ3.51–4.53 (8H in total, *m*, sugar-H), 7.16, 7.17, 7.18 (4H in total, each *s*, galloyl-H). ^{13}C NMR (Me_2CO-d_6 + D_2O): δ64.7–85.6 (sugar C), 95.6, 98.3, 102.0, 105.9 (anomeric C), 110.8 (galloyl C-2,6), 121.4 (galloyl C-1), 138.9 (galloyl C-4), 146.0 (galloyl C-3,5), 166.9, 167.3 (–COO–). (Found: C, 45.90; H, 4.76. $C_{21}H_{22}O_{15}\cdot 2H_2O$ requires: C, 45.1; H, 4.76%.)

Hydrolysis of **1**. Compound **1** (100 mg) was heated with 5% H_2SO_4 at 90° for 14 hr. The soln was neutralized with $BaCO_3$ and the inorganic ppt. filtered off. The filtrate was subjected to Sephadex LH-20 CC with H_2O to give a hydrolysate (**1a**, 25 mg), $[\alpha]_D^{20}$ −91° (H_2O; *c* 0.7). The R_t (12.0 min) and R_f (0.22; silica gel 60, $CHCl_3$–MeOH–H_2O, 14:6:1) coincided with those of 2,7-anhydro-β-D-sedoheptulose (**1a**). Successive elution of the above Sephadex LH-20 column with EtOH yielded gallic acid (12 mg).

Partial hydrolysis of **1**. Compound **1** (20 mg) was heated with 0.2 M HCl at 90° for 5 hr. The reaction mixture was subjected to CC over Sephadex LH-20 using H_2O-MeOH (2:3) to give gallic acid and a hydrolysate (**1b**, 7 mg) as a tan amorphous powder, $[\alpha]_D^{20}$ −304.3° (Me_2CO; *c* 0.2). Negative FABMS: *m/z* 343 $[M-H]^-$. ^1H NMR (Me_2CO-d_6 + D_2O): 3.77 (1H, *dd*, *J* = 4.5 and 8.5 Hz, H-4), 3.93 (1H, *dd*, *J* = 2.5 and 4.3 Hz, H-5), 4.34 (1H, *d*, *J* = 11.9 Hz, H-1), 4.54 (1H, *d*, *J* = 11.9 Hz, H-1), 4.65 (1H, *dd*, *J* = 2.3 and 4.3 Hz, H-6), 7.16 (2H, *s*, galloyl-H). (Found: C, 42.78; H, 5.13. $C_{14}H_{16}O_{10}\cdot 3H_2O$ requires: C, 42.26; H, 5.13%.)

Osazone derivative (**1c**). A mixture of **1** (50 mg), phenylhydrazine·HCl (100 mg) and NaOAc (150 mg) in H_2O (2 ml) was heated at 80° for 30 min. After cooling, the resulting yellow ppt. was collected by filtration and crystallized from H_2O to give the osazone derivative (**1c**, 11 mg) as yellow needles (H_2O), mp 211–212°, $[\alpha]_D^{20}$ +27.3° (Me_2CO; *c* 0.7). Positive FABMS *m/z*: 541 $[M+H]^+$. ^1H NMR (DMSO-d_6 + D_2O): δ3.65 (1H, *m*, H-4), 3.73 (1H, *m*, H-5), 4.00 (1H, *br d*, *J* = 4.6 Hz, H-6), 4.23 (1H, *dd*, *J* = 7.6 and 11.4 Hz, H-7), 4.33 (1H, *dd*, *J* = 2.4 and 11.4 Hz, H-7), 4.56 (1H, *dd*, *J* = 2.0 and 5.1 Hz, H-3), 4.85 (1H, *d*, *J* = 6.6 Hz, 4-OH), 4.95 (1H, *d*, *J* = 5.9 Hz, 5-OH), 5.02 (1H, *d*, *J* = 5.3 Hz, 6-OH), 5.19 (1H, *d*, *J* = 5.1 Hz, 3-OH), 7.00 (2H, *s*, galloyl-H), 7.10–7.40 (10H, in total, *m*, aromatic-H). Found: C, 55.22; H, 5.37; N, 10.03. $C_{26}H_{28}O_9N_4\cdot 3/2H_2O$ requires: C, 54.92; H, 5.47; N, 9.85%.)

2,3-*Di*-O-*galloyl*-D-*glucopyranose* (**2**). An off-white amorphous powder, $[\alpha]_D^{23}$ +133° (Me_2CO; *c*, 0.5). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.96 (*dd*, *J* = 4 and 8 Hz, α-H-2), 5.10 (*t*, *J* = 8 Hz, β-H-2), 5.40 (*t*, *J* = 9 Hz, β-H-3), 5.41 (*d*, *J* = 8 Hz, β-H-1), 5.48 (*d*, *J* = 4 Hz, α-H-1), 5.76 (*t*, *J* = 9 Hz, α-H-3), 7.05, 7.07, 7.11 (each *s*, galloyl-H).

1,2-*Di*-O-*galloyl*-β-D-*glucopyranose* (**3**). Colourless needles

(H_2O), mp 169–170°, $[\alpha]_D^{17} -79.1°$ (Me_2CO; *c* 0.7). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.96 (1H, *t*, $J = 8$ Hz, H-2), 5.88 (1H, *d*, $J = 8$ Hz, H-1), 7.08, 7.11 (each 2H, *s*, galloyl-H).

3,4,6-*Tri*-O-*galloyl*-D-*glucopyranose* (**4**). A tan amorphous powder, $[\alpha]_D^{20} -77.4°$ (MeOH; *c* 1.06). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.20 (*dd*, $J = 4$ and 12 Hz, H-6), 4.40 (*d*, $J = 12$ Hz, H-6), 4.87 (*d*, $J = 8$ Hz, β-H-1), 5.36, 5.41 (each *t*, $J = 9$ Hz, H-4), 5.50 (*d*, $J = 4$ Hz, α-H-1), 5.70 (*t*, $J = 9$ Hz, H-3), 7.04, 7.05, 7.07, 7.16, 7.17 (each *s*, galloyl-H).

1,2,6-*Tri*-O-*galloyl*-β-D-*glucopyranose* (**5**). Colourless needles (H_2O), mp 229–232°, $[\alpha]_D^{20} -85.0°$ (Me_2CO + D_2O; *c* 0.7). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.38 (1H, *dd*, $J = 6$ and 12 Hz, H-6), 4.55 (1H, *d*, $J = 12$ Hz, H-6), 5.22 (1H, *t*, $J = 8$ Hz, H-2), 5.90 (1H, *d*, $J = 8$ Hz, H-1).

1,2,4,6-*Tetra*-O-*galloyl*-β-D-*glucopyranose* (**6**). A white powder (H_2O), $[\alpha]_D^{22} -4.8°$ (Me_2CO; *c* 0.7). ^1H NMR (Me_2CO-d_6 + D_2O): δ5.43 (2H, *t*, $J = 9$ Hz, H-2,4), 6.14 (1H, *d*, $J = 8$ Hz, H-1), 7.10, 7.12, 7.18 (8H, in total, each *s*, galloyl-H).

1,2,3,6-*Tetra*-O-*galloyl*-β-D-*glucopyranose* (**7**). Colourless needles (H_2O), mp 198–200° (dec.), $[\alpha]_D^{24} +35.9°$ (Me_2CO; *c* 0.7). ^1H NMR (Me_2CO-d_6 + D_2O): δ5.50 (1H, *t*, $J = 8$ Hz, H-2), 5.72 (1H, *t*, each 2H, *s*, galloyl-H).

3-O-*Galloyl*-4,6-(S)-*hexahydroxydiphenoyl*-D-*glucose* (**8**). A tan amorphous powder, $[\alpha]_D^{25} +40.6°$ (Me_2CO; *c* 0.7). ^1H NMR (Me_2CO-d_6 + D_2O): δ6.46, 6.64 (each *s*, hexahydroxydiphenoyl-H), 7.04 (2H, *s*, galloyl-H).

2-O-*Galloyl*-4,6-(S)-*hexahydroxydiphenoyl*-D-*glucose* (**9**). A tan amorphous powder, $[\alpha]_D^{26} +62.1°$ (Me_2CO; *c* 0.63). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.91 (*dd*, $J = 4$ and 9 Hz, α-H-2), 5.46 (*d*, $J = 4$ Hz, α-H-1), 6.62, 6.64, 6.72, 6.75 (each *s*, hexahydroxydiphenoyl-H), 7.16, 7.17 (each *s*, galloyl-H).

1-O-*Galloyl*-4,6-(S)-*hexahydroxydiphenoyl*-α-D-*glucose* (**10**). A tan amorphous powder, $[\alpha]_D^{22} +54.9°$ (Me_2CO; *c* 0.4). ^1H NMR (Me_2CO-d_6 + D_2O): δ3.60–4.48 (3H, in total, *m*, H-2,3,5), 3.77 (1H, *d*, $J = 13$ Hz, H-6), 4.93 (1H, *t*, $J = 10$ Hz, H-4), 5.17 (1H, *dd*, $J = 6$ and 13 Hz, H-6), 6.34 (1H, *d*, $J = 4$ Hz, H-1), 6.63, 6.78 (each 1H, *s*, hexahydroxydiphenoyl-H), 7.23 (2H, *s*, galloyl-H).

1-O-*Galloyl*-4,6-(S)-*hexahydroxydiphenoyl*-β-D-*glucose* (**11**). A tan amorphous powder, $[\alpha]_D^{22} -61.0°$ (MeOH; *c* 0.6). ^1H NMR (Me_2CO-d_6 + D_2O): δ4.91 (1H, *t*, $J = 9$ Hz, H-4), 5.21 (1H, *dd*, $J = 6$ and 12 Hz, H-6), 5.76 (1H, *d*, $J = 8$ Hz, H-1), 6.60, 6.72 (each 1H, *s*, hexahydroxydiphenoyl-H), 7.20 (2H, *s*, galloyl-H).

Coriarin F (**12**). An off-white amorphous powder, $[\alpha]_D^{20} +82.0°$ (MeOH; *c* 0.1). ^1H NMR (Me_2CO-d_6 + D_2O): δ3.65 (*d*, $J = 13$ Hz, H-6), 4.51 (*dd*, $J = 7$ and 10 Hz, α-H-5), 4.71 (*d*, $J = 8$ Hz, β-H-1), 4.88 (*t*, $J = 9$ Hz, H-4), 5.08 (*t*, $J = 9$ Hz, β-H-3), 5.15 (*dd*, $J = 7$ and 13 Hz, H-6), 5.25 (*d*, $J = 4$ Hz, α-H-1), 5.37 (*t*, $J = 10$ Hz, α-H-3), 6.47, 6.52, 6.62, 6.63, 7.10, 7.12 (each *s*, valoneayl-H), 6.98 (*s*, galloyl-H).

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