Tannins and Related Compounds. XCVI.[1] Structures of Macaranins and Macarinins, New Hydrolyzable Tannins Possessing Macaranoyl and Tergalloyl Ester Groups, from the Leaves of *Macaranga sinensis* (BAILL.) MUELL.-ARG.

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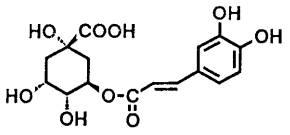
Together with eleven known compounds (1—11), seven new tannins, 3-desgalloylterchebin (12), macaranins A, B and C, and macarinins A, B and C, have been isolated from the leaves of *Macaranga sinensis* (BAILL.) MUELL.-ARG. (Euphorbiaceae). Macaranins A (14), B (13) and C (17) have been determined on the basis of chemical and spectroscopic evidence to be hydrolyzable tannins possessing a novel acyl group (macaranoyl group) at the 3,6-positions of the $^1C_4$ (or skew boat) β-D-glucopyranose ring, while macarinins A (18), B (15) and C (16) were characterized as those having a tergalloyl group at the same positions.

Keywords *Macaranga sinensis*; Euphorbiaceae; hydrolyzable tannin; macaranin; macarinin; macaranic acid; tergallic acid; chebulic acid; dehydrohexahydroxydiphenic acid; putranjivaic acid

In a previous paper,[2] we reported on the characterization of twenty-eight hydrolyzable tannins isolated from the leaves of *Macaranga tanarius* (L.) MUELL.-ARG. As part of our chemical studies on tannins in Euphorbiaceous plants, we next examined *Macaranga sinensis* (BAILL.) MUELL.-ARG., which grows in limited Southeast Asian districts (North Phillipines and Taiwan). As a result, we have isolated seven new hydrolyzable tannins (**12**—**18**), together with eleven known compounds (**1**—**11**). In this paper, we describe the structural elucidation of these compounds.

The aqueous acetone extract of the dried leaves of *M. sinensis* was initially fractionated by Sephadex LH-20 chromatography. Each fraction was subsequently subjected to a combination of chromatographies (Sephadex LH-20, MCI-gel CHP 20P, *etc.*) as described in the experimental section to afford compounds **1**—**18**. Among them, compounds **1**—**11** were identified as chlorogenic acid (**1**),[3] tergallic acid bislactone (**2**),[4] 1,2,4,6-tetra-*O*-galloyl-β-D-glucose (**3**),[5] 3,6-*O*-(*R*)-hexahydroxydiphenoyl (HHDP)-D-glucose (**4**),[6] corilagin (**5**),[7] tercatain (**6**),[4] mallorepanin (**7**),[8] chebulagic acid (**8**),[9] furosin (**9**),[10] geraniin (**10**)[11] and putranjivain A (**11**),[12] by comparisons of their physical



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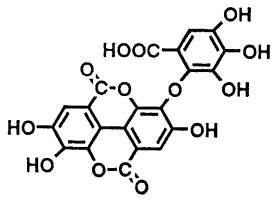

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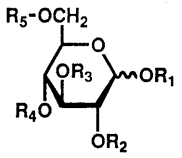
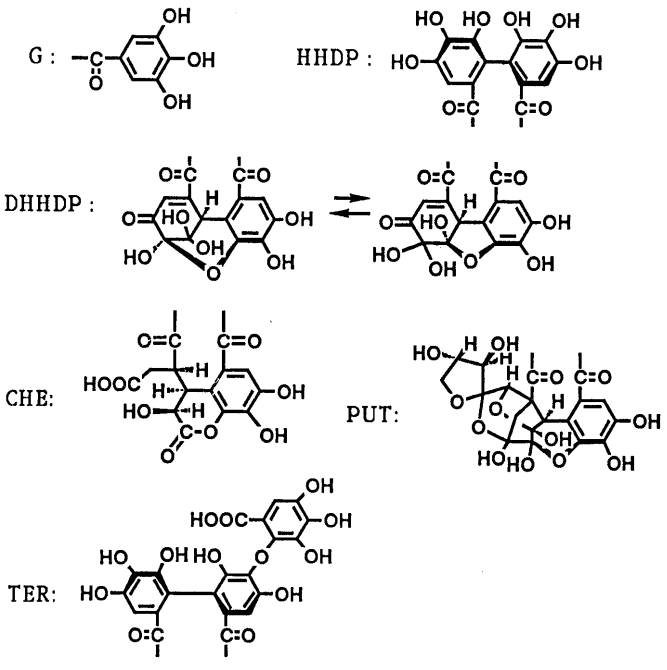


	R_1	R_2	R_4	R_3	R_5
3	(β)G	G	G	H	G
4	H	H	H	HHDP	
5	(β)G	H	H	HHDP	
6	(β)G	H	G	HHDP	
7	(β)G	H	H	TER	
8	(β)G	CHE		HHDP	
9	(β)G	DHHDP		H	H
10	(β)G	DHHDP		HHDP	
11	(β)G	PUT		HHDP	



and spectral data with those of authentic samples.

The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of compound **12** was duplicated owing to the presence of two equilibrium forms of a dehydrohexahydroxydiphenoyl (DHHDP) group [δ 4.98 (1/3H, d, J=2 Hz), 5.30 (2/3H, s), benzylmethine H; 6.26 (1/3H, d, J=2 Hz), 6.54 (2/3H, s, olefinic H].[11] The observation of four aromatic singlets [δ 7.06, 7.08, 7.23, 7.24; 4H in total] suggested the presence of two galloyl groups. The sugar was identified as glucose by acid hydrolysis. The results of negative ion fast atom bombardment mass spectrometry (FAB-MS), which showed the $[M-H]^-$ ion peak at m/z 801, were consistent with a di-*O*-galloyl-DHHDP-glucose structure.

When treated with *o*-phenylenediamine in an acid medium, **12** yielded a phenazine derivative (**12a**). The ^{1}H-NMR spectrum of **12a** clearly showed lowfield shifts of the glucose signals due to H-1 [δ 6.21 (d, J=5 Hz)], H-2 [δ 5.42 (d, J=5 Hz)], H-4 [δ 5.16 (d, J=4 Hz)] and H-6 [δ 4.60—4.95 (m)], as compared with those of glucose, indicating that the hydroxyl groups at these positions are acylated. On heating in hot water, **12a** yielded 1,6-di-*O*-galloyl-β-D-glucopyranose (**12c**),[13] together with a phenazine bislactone (**12b**), thus confirming the allocations of the acyl groups.

The orientation and configuration of the 2,4-substituted DHHDP group were found to be the same as those of furosin (**9**) based on the upfield shift of the anomeric proton signal (δ 6.21) in **12a** as compared with that of **12** (δ 6.53).[14] On the basis of these results, the structure of **12** was established as 1,6-di-*O*-galloyl-2,4-*O*-(*R*)-DHHDP-β-D-glucopyranose (3-desgalloylterchebin).

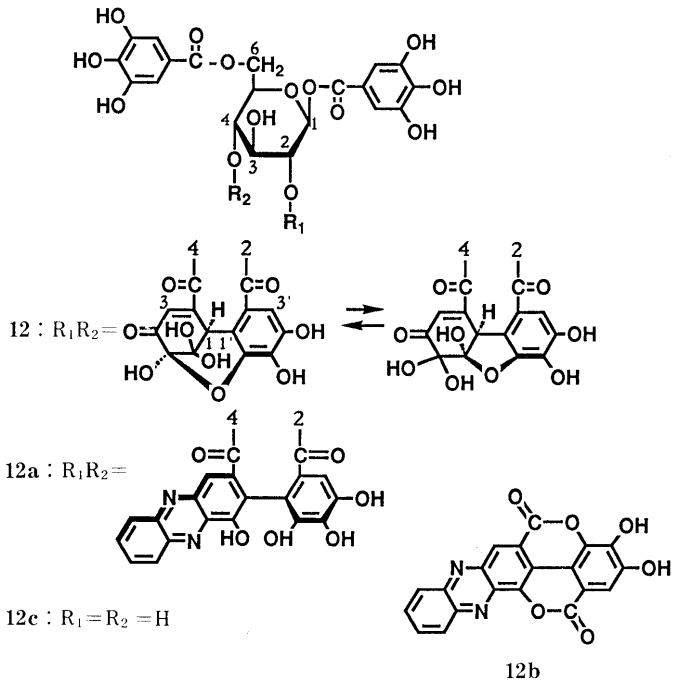
The ^{1}H-NMR spectrum of compound **13** (named macaranin B) showed sugar signals whose chemical shifts and coupling patterns were almost identical with those of corilagin (**5**). In the aromatic region, three one-proton singlet signals (δ 6.74, 6.98, and 7.03) were observed, together with a galloyl singlet [δ 7.10 (2H, s)]. Taking the negative FAB-MS data (m/z 801 $[M-H]^-$) into account, these one-proton signals were considered to be due to a triphenoyl ester group.

Methylation of **13** with ethereal diazomethane gave the dodecamethylate (**13a**) (field desorption mass spectrum (FD-MS) m/z: 971 $[M+H]^+$). Alkaline hydrolysis of **13a**, followed by methylation with diazomethane, afforded methyl 3,4,5-trimethoxybenzoate (**13c**) and an unknown phenolcarboxylic acid methylate (**13b**). In the electron impact mass spectrum (EI-MS), **13b** showed the M^+ peak at m/z 660, which is the same as those of the hitherto known triphenoic acids, trimethyl octa-*O*-methyltergallate (**15b**) and trimethyl octa-*O*-methyl-valoneate (**13g**). Accordingly, the structure **13b** was considered for this phenolcarboxylic acid methylate. Final structural confirmation was obtained by synthesis of racemic **13b** (**13b'**) from gallic acid through Ulmann condensation as shown in Chart 1.[15]

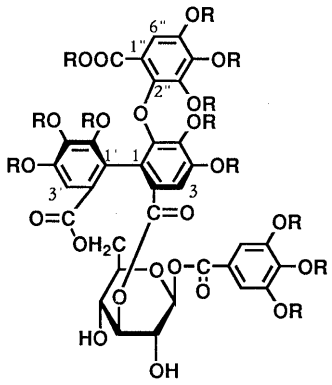
The EI-MS of **13a** showed fragment ions at m/z 614 and 570 which were derived from the macaranoyl group. The formation of the characteristic acid anhydride ion (m/z 614), as well as its decarboxylated ion (m/z 570), indicated that the macaranoyl ester groups are linked to the sugar through the biphenyl carboxyl groups, and that the carboxyl group in the branched aromatic ring exists as a free acid in **13**.

The orientation of the macaranoyl group was concluded to be as shown in the formula **13** based on the ^{1}H-NMR lowfield shifts of the glucose H-6 ($\Delta\delta$ 0.12) in **13** as compared with corilagin (**5**),[16] while the atropisomerism of the biphenyl bond in **13** was determined to be in the *R*-series by comparison of the circular dichroism (CD) spectrum of **13b** with that of (*R*)-trimethyl octa-*O*-methyltergallate (**15b**) (Fig. 1).

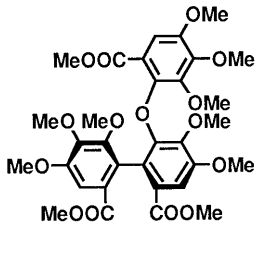
From these findings, macaranin B was characterized as



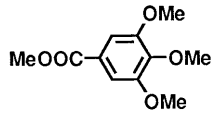
12b



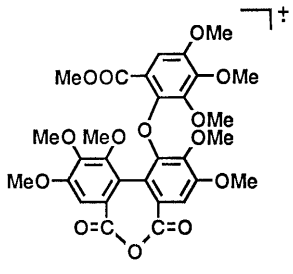
13 : R=H
13a : R=CH3



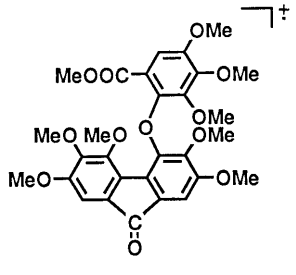
13b



13c



m/z 614



m/z 570

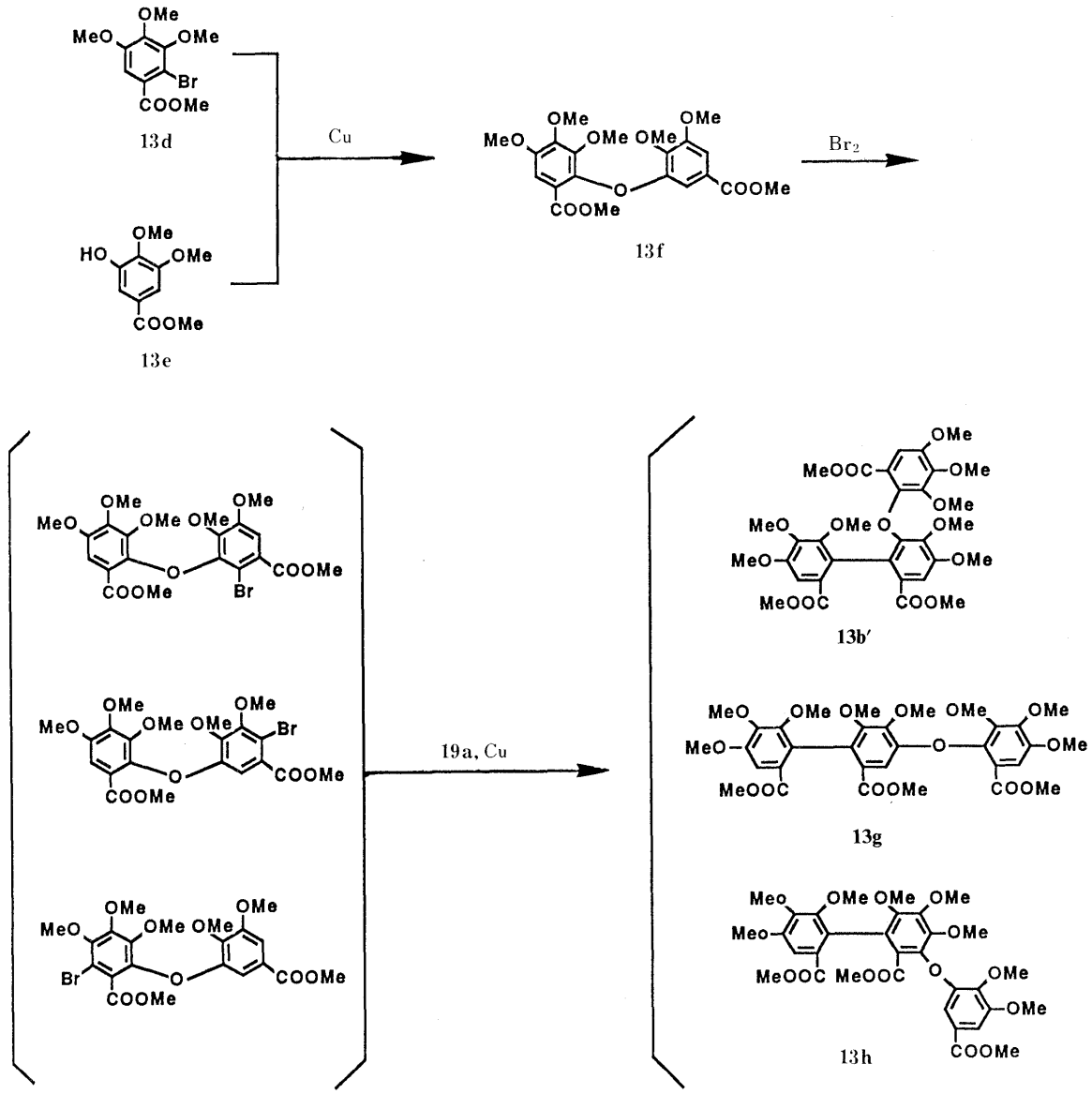


Chart 1

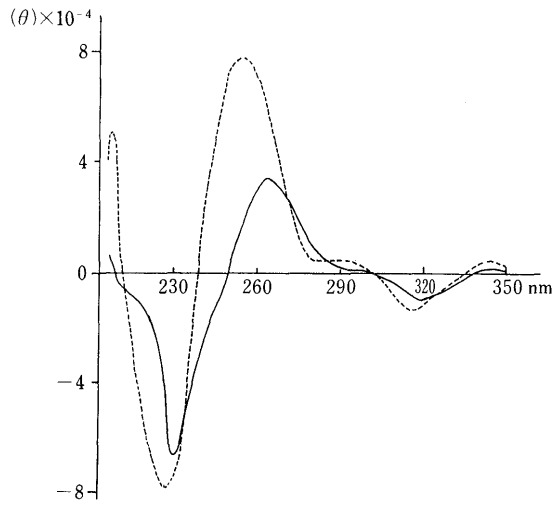


Fig. 1. The CD Spectra of (*R*)-Trimethyl Octa-*O*-methyl-macaranoate (**13b**) and (*R*)-Trimethyl Octa-*O*-methyltergallate (**15b**)
——, **13b**; – – –, **15b**.

1-*O*-galloyl-3,6-*O*-(*R*)-macaranoyl-β-D-glucopyranose (**13**).

The ^{1}H-NMR spectra of compounds **14** (macaranin A) and **15** (macarinin B) were closely related to each other, and showed signals due to a chebuloyl group [**14**: δ 2.19 (2H, d, J=8 Hz), 3.89 (1H, dt, J=2, 8 Hz), 4.95 (1H, d, J=7 Hz), 5.14 (1H, dd, J=2, 7 Hz) and 7.53 (1H, s); **15**: δ 2.18 (2H, d, J=8 Hz), 3.88 (1H, dt, J=2, 8 Hz), 4.90 (1H, d, J=7 Hz), 5.11 (1H, dd, J=2, 7 Hz) and 7.52 (1H, s)] and a galloyl group [**14**: δ 7.14 (2H, s); **15**: δ 7.19 (2H, s)]. The sugar signal patterns in **14** and **15** were also similar, and they were almost identical with those of chebulagic acid (**8**). The observation of three aromatic one-proton singlets [**14**: δ 6.72, 7.01, 7.20; **15**: δ 6.73, 6.96, 7.00] in each case suggested the presence of a triphenoyl acyl group, in accordance with the negative FAB-MS of **14** and **15**, exhibiting the same $[M-H]^-$ ion peak at m/z 1121.

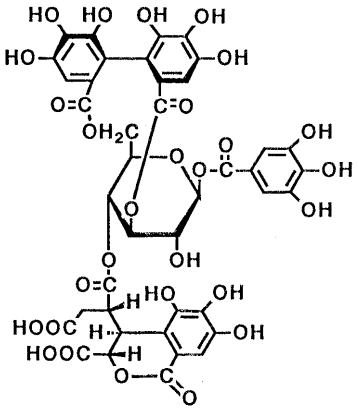
On methylation with dimethyl sulfate and potassium carbonate in dry acetone, **14** and **15** afforded the respective heptadecamethylates (**14a** and **15a**). Subsequent alkaline hydrolysis, followed by diazomethane methylation, yielded (*R*)-trimethyl octa-*O*-methylmacaranate (**13b**) $[\alpha]_D$ −4.7°

($CHCl_3$)] and (*R*)-trimethyl octa-*O*-methyltergallate (**15b**),[17] respectively, together with methyl 3,4,5-trimethoxybenzoate (**13c**) and trimethyl tri-*O*-methylchebulate (**14b**).

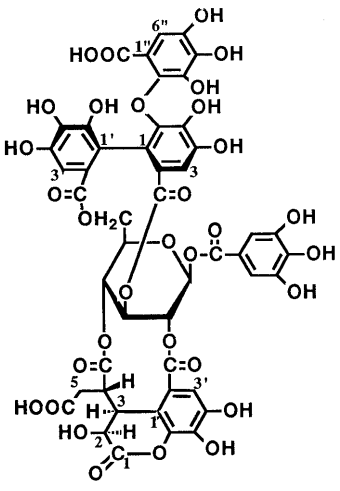
The locations of acyl groups in the glucose moiety were determined in the following manner. Compound **14** was treated with hot water to yield macaranin B (**13**) and a partial hydrolysate (**14c**). The production of **13** thus confirmed the locations of the galloyl and macaranoyl groups. The ^{1}H-NMR spectrum of **14c** showed an upfield shift of the glucose H-2 signal (δ 4.25) as compared with that (δ 5.48) in **14**. Furthermore, the chemical shifts and coupling patterns of the signals due to the chebuloyl group were found to be almost identical with those of neochebulagic acid (**8a**), which was obtained by similar partial hydrolysis of **8**.[18] These observations indicated that the orientation of the chebuloyl group at the glucose C-2 and C-4 positions in **14** is the same as that of **8**.

Similarly, treatment of **15** in hot water afforded mallorepanin (**7**) and a partial hydrolysate (**15c**). The ^{1}H-NMR spectrum of **15c** was closely correlated with that of **14c**, except for the chemical shifts of the three aromatic singlets, confirming the locations of the acyl groups.

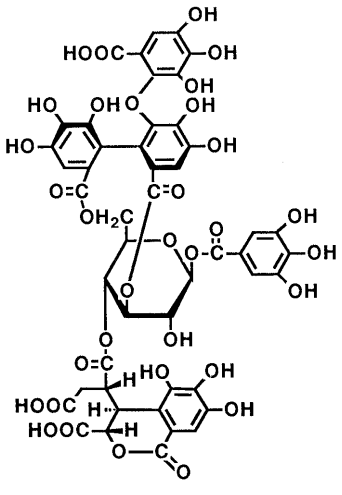
The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **15** showed eight carboxyl carbon signals, among which signals at δ 166.2, 168.8 and 170.9 were attributed to the C-7, C-7′ and C-7″ carboxyl carbons, respectively, in the tergalloyl moiety by ^{1}H–^{13}C long-range shift correlation spectroscopy (^{1}H–^{13}C long-range COSY) (Fig. 2). Namely, first of all, the signals at δ 173.6, 173.2 and 169.8 were readily assignable to the carboxyl carbons in the chebuloyl moiety, since they were found to be coupled with the chebuloyl aliphatic protons (H-5, H-2 and H-3). Next, the two upfield signals at δ 165.4 and 165.6 were attributed to the galloyl and chebuloyl aromatic carboxyl carbons, respectively, based on their long-range couplings with the corresponding aromatic protons. Thus, the remaining signals at δ 166.2, 168.8 and 170.9 were attributable to the tergalloyl ester carbons. Among these signals, the signal at δ 170.9 was concluded to be due to the carboxylic acid carbon (C-7″) from its broadness and its appearance as a doublet in the off-resonance spectrum (Fig. 3). The observation of cross peaks between the aromatic proton signal at δ 6.73 and carbon signals at δ 144.8 and 136.4, whose chemical shifts were almost identical with those of the respective C-4 and C-5 carbons in the HHDP group, indicated this proton signal to be assignable to the proton of the aromatic ring having no branched gallic acid moiety. Since this aromatic proton signal was further correlated with the carboxyl carbon signal at δ 168.8, this carboxyl signal could be assigned to C-7′. Therefore, the remaining signal at δ 166.2 was attributed to C-7. In the non-decoupling mode (Fig. 3), the C-7′ signal (δ 168.8) appeared as a multiplet, and this signal was changed into a doublet when the glucose H-6 signal (δ 4.70) was irradiated. This clearly indicated the orientation of the tergalloyl group to be as shown in the formula **15**.



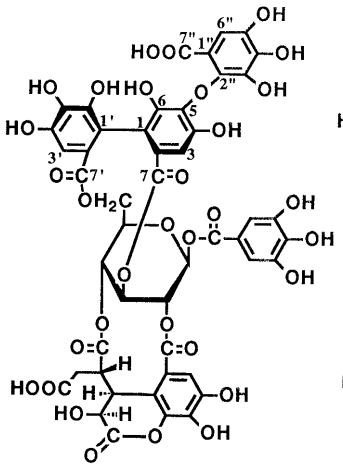
8a



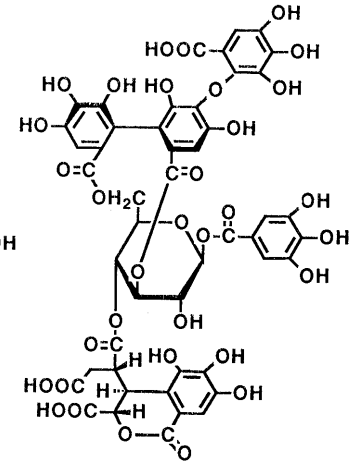
14



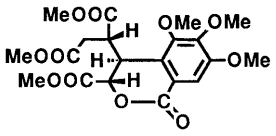
14c



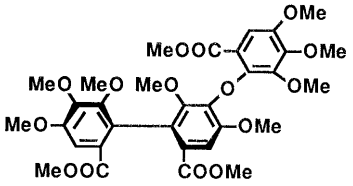
15



15c



14b



15b

On the basis of these findings, the structures of macaranin A and macarinin B were established as 1-*O*-galloyl-2,4-*O*-chebuloyl-3,6-*O*-(*R*)-macaranoyl-*β*-D-glucopyranose (**14**) and 1-*O*-galloyl-2,4-*O*-chebuloyl-3,6-*O*-(*R*)-tergalloyl-*β*-D-glucopyranose (**15**), respectively.

The negative FAB-MS of compound **16** (macarinin C) exhibited the $[M-H]^-$ ion peak at *m/z* 1103 which is 18 mass units smaller than that of **15**. The ^{1}H- and ^{13}C-NMR spectra differed from those of **15** only in the chemical shifts of the aromatic signals arising from the triphenoyl moiety. In particular, the carbon signals due to the C-7″ carboxyl group and C-6 were observed at upper field, whereas the C-1, C-3 and C-5 signals were shifted to lower field (Table I) as compared with those of **15**, thus indicating the formation of a lactone ring through the C-6 oxygen and the C-7″ carboxyl group. Accordingly, the structure of macarinin C was concluded to be as represented by the formula **16**. It remains unclear whether macarinin C is

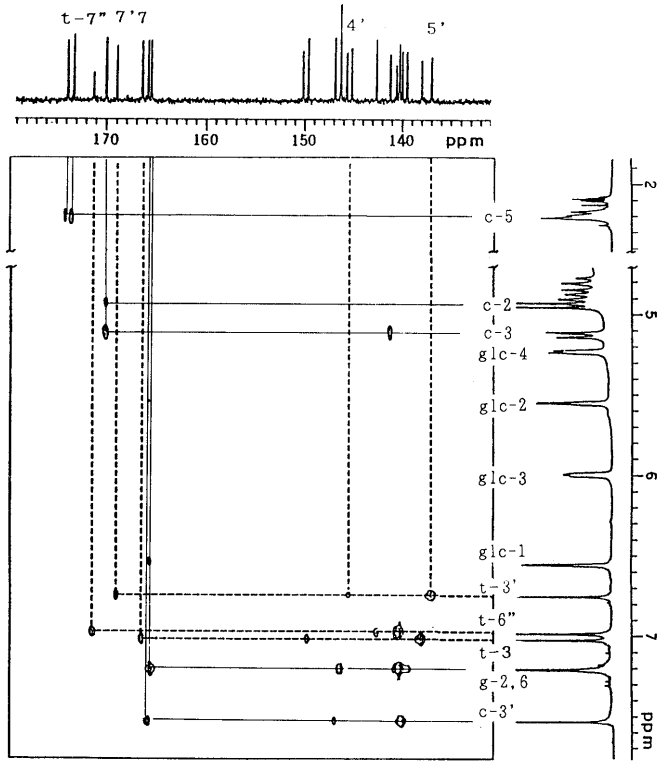


Fig. 2. The ^{1}H–^{13}C Long-Range COSY Spectrum of **15** in Acetone-d_6+D_2O (J_{CH}=10 Hz)

glc, glucose; t, tergalloyl; c, chebuloyl; g, galloyl.

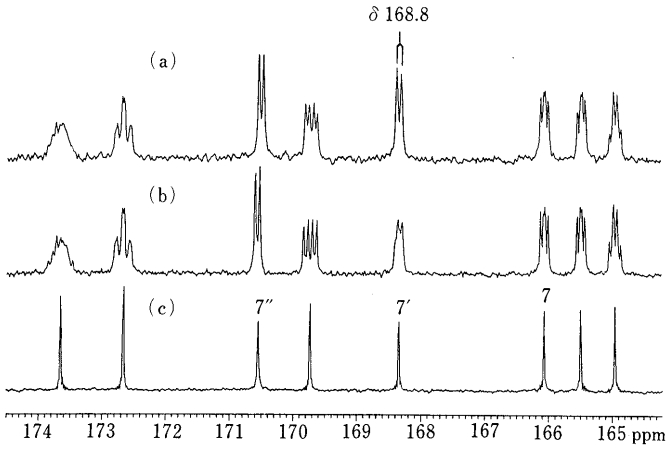
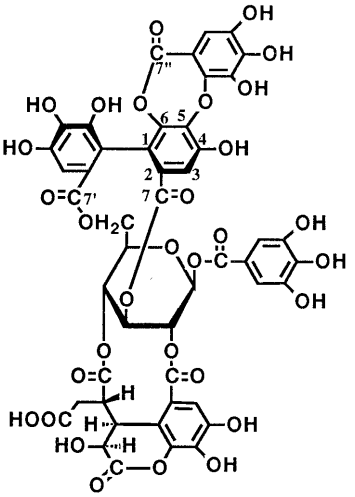
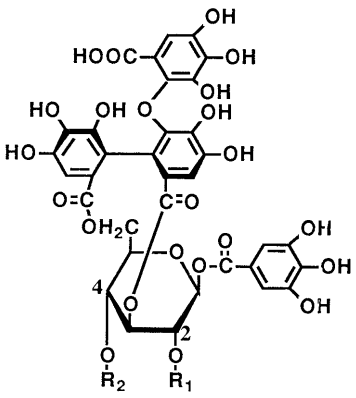


Fig. 3. Long-Range Selective Proton-Decoupling (LSPD) Experiments in **15**

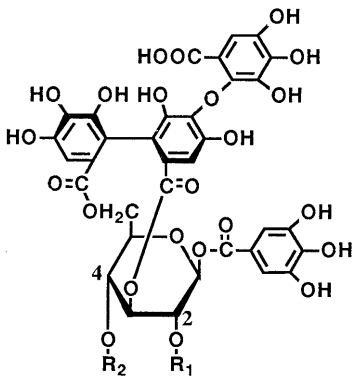
a) Irradiation at *δ* 4.70 (glc H-6). b) Non-decoupling. c) Complete decoupling



16

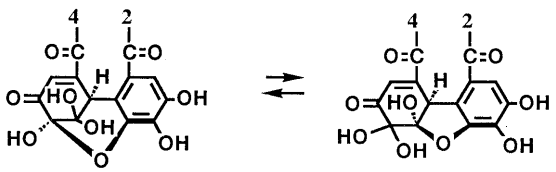


17, 17a



18, 18a

17, 18: R_1, R_2 =



17a, 18a: R_1, R_2 =

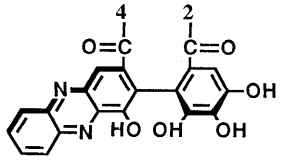


TABLE I. ^{13}C-NMR Data for the Triphenoyl Moieties in Macarinin B (**15**) and Macarinin C (**16**)[a]

	1	2	3	4	5	6	7″
15	116.7	129.8	110.1	149.2	137.7	149.8	170.9
16	122.0	130.5	114.8	148.5	143.9	145.3	163.5
$\Delta\delta$	+5.3	+0.7	+4.9	−0.7	+6.2	−4.5	−7.4

a) The assignments of these signals were based on the ^{1}H–^{13}C long-range COSY spectrum.

formed from the major tannin, macarinin B, during the isolation procedure.

Compounds **17** (macaranin C) and **18** (macarinin A) showed the same $[M-H]^-$ ion peak at *m/z* 1119 in the negative FAB-MS. The ^{1}H-NMR spectra of **17** and **18** showed the presence of equilibrium forms of DHHDP groups [**17**: δ 4.94 (1/3H, d, $J=2$ Hz), 5.16 (2/3H, s), benzylmethine H, δ 6.26 (1/3H, d, $J=2$ Hz), 6.54 (2/3H, s), olefinic H; **18**: δ 4.94 (1/3H, d, $J=2$ Hz), 5.17 (2/3H, s), benzylmethine H, δ 6.25 (1/3H, d, $J=2$ Hz), 6.53 (2/3H, s), olefinic H]. The chemical shifts and coupling patterns of the sugar signals resembled those of geraniin (**10**), suggesting similar substitution patterns in the glucose moiety.

When treated with *o*-phenylenediamine in acetic acid, **17** and **18** afforded the phenazine derivatives (**17a** and **18a**), (negative FAB-MS *m/z*: 1173 $[M-H]^-$). On partial hydrolysis in hot water, **17a** and **18a** yielded 1-*O*-galloyl-3,6-*O*-(*R*)-macaranoyl-β-D-glucose (**13**) and 1-*O*-galloyl-3,6-*O*-(*R*)-tergalloyl-β-D-glucose (**7**), respectively, together with the phenazine bislactone (**12b**). In the ^{1}H-NMR spectra of **17a** and **18a**, the upfield shifts (**17a**: $\Delta\delta$ 0.42; **18a**: $\Delta\delta$ 0.37) of anomeric proton signals[14] indicated the absolute configuration of the DHHDP group to be in the *R*-series. Therefore, macaranin C was characterized as 1-*O*-galloyl-2,4-*O*-(*R*)-DHHDP-3,6-*O*-(*R*)-macaranoyl-β-D-glucopyranose (**17**) and macarinin A as 1-*O*-galloyl-2,4-*O*-(*R*)-DHHDP-3,6-*O*-(*R*)-tergalloyl-β-D-glucopyranose (**18**).

Macaranins A (**14**), B (**13**) and C (**17**) represent the first examples of hydrolyzable tannins which possess the novel acyl group, macaranoyl group. A notable feature of the hydrolyzable tannins in this plant is the absence of tannins having a valoneayl group, which is very commonly found in nature.

Experimental

Details of the instruments and chromatographic conditions used throughout this work are the same as described in the the previous paper.[2]

Extraction and Isolation Dried leaves of *Macaranga sinensis* (5.6 kg), collected at Lanyu Island, Taiwan, Republic of China, were extracted three times with 70% acetone at room temperature. After removal of acetone by evaporation under reduced pressure, the resulting precipitates, consisting mainly of chlorophylls and waxes, were removed by filtration. The filtrate was chromatographed over Sephadex LH-20, and elution was carried out with H_2O containing an increasing amount of MeOH and finally with 50% aqueous acetone to give three fractions, fr. I (180 g), fr. II (237 g) and fr. III (78 g).

Fraction I was subjected to repeated chromatographies over MCI-gel CHP 20P and Fuji-gel ODS G-3 with H_2O containing increasing amounts of MeOH and over Sephadex LH-20 with EtOH and 60% MeOH to yield chlorogenic acid (**1**) (60 mg), tergallic acid dilactone (**2**) (20 mg) and corilagin (**5**) (300 mg). Repeated chromatography of fr. II over MCI-gel CHP 20P, Bondapak C_{18}/Porasil B with H_2O containing increasing amount of MeOH and Sephadex LH-20 with EtOH and 60% or 80% MeOH afforded 3,6-*O*-(*R*)-HHDP-D-glucose (**4**) (180 mg), tercatain (**6**) (16.7 mg), mallorepanin (**7**) (130 mg), chebulagic acid (**8**) (190 mg), furosin (**9**) (240 mg), geraniin (**10**) (6.03 g), putranjivain A (**11**) (180 mg) and compound **12** (270 mg), macaranin B (**13**) (160 mg), macarinin B (**15**) (4.02 g) and macarinin A (**18**) (2.36 g). On similar separation, Fraction III yielded 1,2,4,6-tetra-*O*-galloyl-β-D-glucose (**3**) (70 mg), macaranin A (**14**) (430 mg), macarinin C (**16**) (420 mg) and macaranin C (**17**) (160 mg).

Compound 12 A yellow crystalline powder (H_2O), mp 243 °C (dec.), $[\alpha]_D^{15}$ −52.9° ($c=1.1$, MeOH). Negative FAB-MS *m/z*: 801 $[M-H]^-$. *Anal.* Calcd for $C_{34}H_{26}O_{23}\cdot 5H_2O$: C, 45.76; H, 4.07. Found: C, 45.71; H, 4.02. ^{1}H-NMR (acetone-d_6+D_2O) δ: 4.45—4.70, 4.80—4.95 (each 2H, m, H-3, 5, 6), 4.98 (1/3H, d, $J=2$ Hz, DHHDP H-1), 5.19 (1H, s-like, H-4), 5.30 (2/3H, s, DHHDP H-1), 5.39 (1H, br s, H-2), 6.26 (1/3H, d, $J=2$ Hz, DHHDP H-3), 6.53 (1H, br s, H-1), 6.54 (2/3H, s, DHHDP H-3), 7.06, 7.08, 7.23, 7.24 (4H in total, galloyl H), 7.26, 7.27 (1H in total, DHHDP H-3′). ^{13}C-NMR (acetone-d_6+D_2O) δ: 45.7, 51.7 (DHHDP C-1), 60.9, 61.7, 65.1, 65.4, 70.6, 71.1, 71.4, 71.7, 74.1, 74.5 (glc C-2—6), 90.9, 91.8 (glc C-1), 92.3, 92.6, 96.1 (DHHDP C-5, 6), 108.8, 113.6, 113.8, 115.8, 117.3, 118.9, 119.7 (DHHDP C-1′, 2′, 3′, 6), 109.9 (2C), 110.3 (2C) (galloyl C-2, 6), 125.6, 128.8 (DHHDP C-3), 137.2, 139.1, 139.7, 143.1, 145.7, 147.5, 149.2, 154.6 (galloyl C-4, DHHDP C-2, 4′, 5′, 6′), 165.3, 165.6, 166.0, 167.0 (–COO–), 192.2, 195.0 (DHHDP C-4).

Acid Hydrolysis of 12 A solution of **12** (8 mg) in 1 N H_2SO_4 (1 ml) was heated at 90 °C for 2 h. After cooling, the reaction mixture was neutralized with Amberlite IRA-400 ion exchange resins. The spot corresponding to glucose was detected by thin layer chromatography (TLC) [*Rf* 0.40, cellulose, *n*-BuOH–pyridine–H_2O (6:4:3); detection, aniline–hydrogen phthalate reagent].

Preparation of Phenazine Derivative (12a) A solution of **12** (35 mg) in EtOH (3 ml) was treated with *o*-phenylenediamine (15 mg) in 20% AcOH–EtOH (4.5 ml), and the mixture was left standing at room temperature for 1.5 h. After removal of EtOH under reduced pressure, the mixture was subjected to Sephadex LH-20 chromatography (EtOH–MeOH) to give **12a** as a tan amorphous powder (27 mg), $[\alpha]_D^{15}$ −98.6° ($c=0.9$, MeOH). Negative FAB-MS *m/z*: 855 $[M-H]^-$. *Anal.* Calcd for $C_{40}H_{28}N_2O_{20}\cdot 2H_2O$: C, 53.81; H, 3.61; N, 3.14. Found: C, 53.53; H, 3.77; N, 2.97. ^{1}H-NMR (acetone-d_6) δ: 4.58 (1H, d, $J=4$ Hz, H-3), 4.60—4.95 (3H, m, H-5, 6), 5.16 (1H, d, $J=4$ Hz, H-4), 5.42 (1H, d, $J=5$ Hz, H-2), 6.21 (1H, d, $J=5$ Hz, H-1), 6.97, 7.17 (each 2H, s, galloyl H), 7.45 [1H, s, phenazine (ph.) H-3′], 8.25 (1H, s, ph. H-3), 7.90—8.41 (4H in total, m, ph. H-3″, 4″, 5″, 6″). ^{13}C-NMR (acetone-d_6) δ: 65.8, 66.5, 72.7, 77.7, 78.8 (glc C-2—6), 92.4 (glc C-1), 110.2 (4C, galloyl C-2, 6), 112.4, 116.3, 116.8, 119.6 (2C), 120.2, 121.3 (galloyl C-1, ph. C-1, 1′, 2′, 3, 3′), 130.1, 130.5 (ph. C-3″, 4″), 132.3 (2C, ph. C-3″, 6″), 136.0, 138.9 (2C), 139.5 (2C) (galloyl C-4, ph. C-2, 5, 5′), 142.7, 143.2 (ph. C-1″, 2″), 145.3 (2C, ph. C-4, 4′), 146.0 (4C, galloyl C-3, 5), 152.1 (ph. C-6), 164.8, 166.5, 167.1, 167.8 (–COO–).

Partial Hydrolysis of 12a in Hot Water A solution of **12a** (7 mg) in H_2O was heated at 90 °C for 3 h. After cooling, the resulting precipitate was collected by filtration and washed with water to afford the brownish phenazine bislactone (**12b**). IR ν_{max}^{KBr} cm^{-1}: 1590, 1610, 1740. After concentration, the filtrate was chromatographed over Sephadex LH-20 with EtOH to give **12c** as an off-white amorphous powder, $[\alpha]_D^{21}$ −21.9° ($c=1.0$, MeOH). ^{1}H-NMR (acetone-d_6) δ: 4.39 (1H, dd, $J=4$, 12 Hz, H-6), 4.56 (1H, dd, $J=2$, 12 Hz, H-6), 5.73 (1H, d, $J=7$ Hz, H-1), 7.13, 7.16 (each 2H, s, galloyl H).

Macaranin B (13) An off-white amorphous powder, $[\alpha]_D^{15}$ −42.2° ($c=1.0$, MeOH). Negative FAB-MS *m/z*: 801 $[M-H]^-$. *Anal.* Calcd for $C_{34}H_{26}O_{23}\cdot 3H_2O$: C, 47.67; H, 3.77. Found: C, 47.58; H, 3.68. ^{1}H-NMR (acetone-d_6+D_2O) δ: 4.09 (1H, br s, H-2), 4.25 (1H, dd, $J=10$, 11 Hz, H-6), 4.48 (1H, br s, H-4), 4.58 (1H, br t, $J=10$ Hz, H-5), 4.86 (1H, br s, H-3), 4.98 (1H, br t, $J=10$ Hz, H-6), 6.41 (1H, d, $J=2$ Hz, H-1), 6.74, 6.98, 7.03 (each 1H, aromatic H), 7.10 (2H, s, galloyl H). ^{13}C-NMR (acetone-d_6+D_2O) δ: 62.1 (glc C-4), 64.5 (glc C-6), 68.6 (glc C-2), 70.8 (glc C-3), 75.5 (glc C-5), 94.5 (glc C-1), 110.7 (2C, galloyl C-2, 6), 145.7 (2C, galloyl C-3, 5), 108.9, 109.4, 112.1, 113.9, 116.3, 119.2, 120.1, 123.8, 125.5 [galloyl C-1, macaranoyl (mac.) C-1, 1′, 1″, 2, 2′, 3, 3′, 6″], 137.2, 139.8 (2C), 139.9 (2C), 140.8, 141.5, 144.3, 145.3, 146.3 (galloyl C-4, mac. C-2″, 3″, 4, 4′, 4″, 5, 5′, 5″, 6, 6′), 166.1, 167.3, 169.7 (–COO–).

Methylation of 13 A solution of **13** (50 mg) in MeOH was treated with ethereal CH_2N_2 at room temperature. After removal of the solvent and excess reagent by evaporation, the residue was chromatographed over silica gel. Elution with benzene–acetone (4:1) afforded a dodecamethylate (**13a**) (24 mg) as a white amorphous powder, $[\alpha]_D^{16}$ −48.8° ($c=1.0$, $CHCl_3$). FD-MS *m/z*: 971 $[M+H]^+$. EI-MS *m/z*(%): 758(36), 632(100), 614(71), 570(84), 212(72). *Anal.* Calcd for $C_{46}H_{50}O_{23}\cdot 2H_2O$: C, 54.86; H, 5.41.

Found: C, 54.85; H, 5.05. ^{1}H-NMR ($CDCl_3$) δ: 3.20, 3.38, 3.71, 3.74, 3.76, 3.86, 3.88, 3.89, 3.90 (each s, 36H in total, OMe), 6.52 (2H, br s, H-1 and aromatic H), 6.80, 7.07 (each 1H, s, aromatic H), 7.26 (2H, s, trimethoxybenzoyl H).

Alkaline Methanolysis of 13a A solution of **13a** (27 mg) in MeOH (2 ml) and 10% NaOH (2 ml) was heated under reflux for 1 h. After removal of MeOH by evaporation under reduced pressure, the mixture was acidified with 10% HCl and extracted with ether. The organic layer was concentrated and the residue was treated at room temperature with ethereal CH_2N_2. Purification of the products by silica gel chromatography (*n*-hexane–acetone, 19 : 1) furnished methyl 3,4,5-trimethoxybenzoate (8.2 mg) and **13b** (9.8 mg). **13b**: a cololrless syrup, $[\alpha]_D^{26}$ $-4.7°$ ($c=1.0$, $CHCl_3$). CD ($c=1.1\times10^{-2}$, MeOH) $[\theta]^{20}$ (nm): $-66{,}000$ (231), $+35{,}000$ (261), $-12{,}000$ (319). EI-MS *m/z*: 660 $(M)^+$. *Anal.* Calcd for $C_{32}H_{36}O_{15}\cdot 3/2H_2O$: C, 55.89; H, 5.72. Found: C, 56.03; H, 5.43. ^{1}H-NMR (acetone-d_6) δ: 3.40, 3.58, 3.62, 3.66, 3.73, 3.78, 3.80, 3.89, 3.90 (each s, 33H in total, OMe), 7.00, 7.27, 7.39 (each 1H, s, aromatic H).

Preparation of Trimethyl Octa-*O*-methylmacaranate (13b′) A mixture of methyl 2-bromo-3,4,5-trimethoxybenzoate (**13d**) (467 mg), methyl 3,4-dimethoxy-5-hydroxybenzoate (**13e**) (307 mg) and copper powder (500 mg) in a sealed tube was heated in an oil bath (120—190 °C for 6 h. The reaction mixture was suspended in chloroform and the insoluble copper powder was removed by filtration. The filtrate, after concentration *in vacuo*, was subjected to silica gel column chromatography, and elution with benzene–acetone (13 : 1) gave dimethyl penta-*O*-methyl-*m*-dehydrodigallate (**13f**),[19] mp 118 °C (MeOH), ^{1}H-NMR (acetone-d_6) δ: 3.76, 3.72, 3.78 (each 3H), 3.93, 3.95 (each 6H), 6.78, 7.31 (each 1H, d, $J=2$ Hz), 7.32 (1H, s). A solution of **13f** (113 mg) in ethanol was treated with bromine at room temperature for 5 min. After addition of 20% $Na_2S_2O_3$ (20 ml), the bromide mixture was extracted with benzene. The organic layer was concentrated to dryness and the residue was mixed with **13d** (250 mg) and copper powder (500 mg) in a sealed tube. After being heated in an oil bath (160—180 °C) for 4 h, the mixture was suspended in chloroform and the copper powder was removed by filtration. The filtrate was concentrated under reduced pressure and chromatographed over silica gel with benzene–acetone (96 : 4—90 : 10) to give compounds **13b′** (4 mg), **13g** (13 mg) and **13h** (9 mg). The ^{1}H-NMR and IR ($CDCl_3$) spectra were identical with those of **13b**, trimethyl octa-*O*-methylvaloneate[20] and trimethyl octa-*O*-methylsanguisobate,[21] respectively.

Macaranin A (14) An off-white amorphous powder, $[\alpha]_D^{15}$ $-43.3°$ ($c=1.1$, MeOH). Negative FAB-MS *m/z*: 1121 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{34}O_{32}\cdot 4H_2O$: C, 48.25; H, 3.54. Found: C, 48.30; H, 3.46. ^{1}H-NMR (acetone-d_6) δ: 2.19 [2H, d, $J=8$ Hz, chebuloyl (che.) H-5], 3.89 (1H, dt, $J=2$, 8 Hz, che. H-4), 4.40—4.55 (1H, m, H-6), 4.76—4.90 (2H, m, H-5, 6), 4.95 (1H, d, $J=7$ Hz, che. H-2), 5.0—5.2 (1H, m, H-4), 5.14 (2H, dd, $J=2$, 7 Hz, che. H-3), 5.48 (1H, br s, H-2), 5.97 (1H, s-like, H-3), 6.54 (1H, s, H-1), 6.72, 7.01, 7.20 (each 1H, s, aromatic H), 7.14 (2H, s, galloyl H), 7.53 (1H, s, che. H-3′). ^{13}C-NMR (acetone-d_6) δ: 30.2 (che. C-5), 39.4 (che. C-4), 41.1 (che. C-3), 61.8 (glc C-3), 64.2 (glc C-6), 66.2, 66.6 (glc C-4, che. C-2), 70.3 (glc C-2), 73.8 (glc C-5), 91.7 (glc C-1), 110.7 (2C, galloyl C-2, 6), 108.8, 109.9, 112.4, 116.0, 116.1, 117.2, 119.0, 120.2, 124.0, 125.0 (galloyl C-1; mac. C-1, 1′, 1″, 2, 2′, 3, 3′, 6″; che. C-1′, 2′, 3′), 137.0, 137.4, 139.5, 139.9, 140.4, 140.9, 141.2, 141.7, 144.6, 145.6, 146.5 (galloyl C-4; mac. C-2″, 3″, 4, 4′, 4″, 5, 5′, 5″, 6, 6′; che. C-4′, 5′, 6′), 146.0 (2C, galloyl C-3, 5), 165.0, 165.5, 166.0, 167.8, 169.7, 172.6, 173.6 (–COO–).

Methylation of 14 A mixture of **14** (165 mg), dimethyl sulfate (2 ml) and anhydrous potassium carbonate (2.0 g) in dry acetone (15 ml) was heated under reflux for 4 h. After removal of the inorganic precipitates by filtration, the filtrate was concentrated to dryness under reduced pressure. The residue was purified by silica gel with benzene–acetone (19 : 1) to afford the heptadecamethylate (**14a**) (69 mg) as a white amorphous powder, $[\alpha]_D^{16}$ $-4.2°$ ($c=1.0$, $CHCl_3$). Positive FAB-MS *m/z*: 1378 $[M]^+$. *Anal.* Calcd for $C_{65}H_{70}O_{33}$: C, 56.60; H, 5.12. Found: C, 56.71; H, 5.49. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 2.36 (1H, dd, $J=18$, 10 Hz, che. H-5), 2.78 (1H, d, $J=10$ Hz, che. OH-2), 2.93 (1H, dd, $J=18$, 4 Hz, che. H-5), 3.34, 3.39, 3.64, 3.72, 3.76, 3.86, 3.88, 3.89, 3.91, 3.99 (each s, 51H in total, OMe), 4.70, 4.72, 4.93 (each 1H, t, $J=9$ Hz, H-5, 6, 6), 4.83 (1H, t, $J=10$ Hz, che. H-2), 5.17 (1H, d, $J=10$ Hz, che. H-3), 5.29 (1H, br s, H-4), 5.45 (1H, s, H-2), 5.81 (1H, br s, H-3), 6.70 (1H, s, H-1), 6.66, 6.78, 7.06 (each 1H, s, aromatic H), 7.31 (2H, s, trimethoxybenzoyl H), 7.44 (1H, s, che. H-3′).

Alkaline Methanolysis of 14a A solution of **14a** (20 mg) in MeOH (2 ml) and 10% NaOH (2 ml) was heated under reflux for 1 h. Work-up as described for **13a** yielded methyl 3,4,5-trimethoxybenzoate (**13c**) (2.2 mg), **13b** (8.7 mg) and **14b** (3.9 mg). **14b**: ^{1}H-NMR ($CDCl_3$) δ: 2.42 (1H, dd, $J=17$, 6 Hz, H-5), 2.79 (1H, dd, $J=17$, 9 Hz, H-5), 3.24 (1H, dt, $J=6$, 9 Hz, H-4), 3.58, 3.65, 3.75, 3.86, 3.91, 3.94 (each 3H, s, OMe), 3.86 (1H, dd, $J=1$, 9 Hz, H-3), 5.25 (1H, d, $J=1$ Hz, H-2), 7.40 (1H, s, aromatic H).

Partial Hydrolysis of 14 in Hot Water A solution of **14** (105 mg) in H_2O (1 ml) was heated at 95 °C for 30 h. The reaction mixture, after having cooled, was chromatographed over Sephadex LH-20 (EtOH) to give **13** (2 mg) and **14c** (32 mg). **14c**: an off-white amorphous powder, $[\alpha]_D^{15}$ $+6.4°$ ($c=1.0$, MeOH). Negative FAB-MS *m/z*: 1139 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{36}O_{33}\cdot 4H_2O$: C, 47.52; H, 3.66. Found: C, 47.13; H, 3.66. ^{1}H-NMR (270 MHz, acetone-d_6+D_2O) δ: 2.48 (1H, dd, $J=17$, 4 Hz, che. H-5), 2.95 (1H, dd, $J=17$, 10 Hz, che. H-5), 4.25 (1H, br s, H-2), 4.40—4.45 (1H, m, che. H-4), 4.65 (1H, d, $J=8$ Hz, H-5, 6), 4.65 (1H, s, che. H-3), 4.80 (1H, m, H-6), 5.00 (1H, d, $J=1$ Hz, H-4), 5.40 (1H, s, che. H-2), 5.66 (1H, d, $J=1$ Hz, H-3), 6.29 (1H, br s, H-1), 6.48, 6.90, 7.04 (each 1H, s, aromatic H), 7.14 (1H, s, che. H-3′), 7.16 (2H, s, galloyl H).

Macarinin B (15) An off-white amorphous powder, $[\alpha]_D^{15}$ $-23.1°$ ($c=1.1$, MeOH). Negative FAB-MS *m/z*: 1121 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{34}O_{32}\cdot 4H_2O$: C, 48.25; H, 3.54. Found: C, 48.58; H, 3.36. ^{1}H-NMR (acetone-d_6+D_2O) δ: 2.18 (2H, d, $J=8$ Hz, che. H-5), 3.88 (1H, dt, $J=2$, 8 Hz, che. H-4), 4.4—4.8 (2H, m, H-6), 4.86 (1H, m, H-5), 4.90 (1H, d, $J=7$ Hz, che. H-2), 5.11 (1H, dd, $J=2$, 7 Hz, che. H-3), 5.20 (1H, m, H-4), 5.52 (1H, br s, H-2), 5.95 (1H, s-like, H-3), 6.51 (1H, br s, H-1), 6.73, 6.96, 7.00 (each 1H, s, aromatic H), 7.19 (2H, s, galloyl H), 7.52 (1H, s, che. H-3′). ^{13}C-NMR (acetone-d_6+D_2O) δ: 91.8 (glc C-1), 71.0 (glc C-2), 62.3 (glc C-3), 66.4 (glc C-4), 74.0 (glc C-5), 64.1 (glc C-6), 119.8 (galloyl C-1), 110.6 (2C, galloyl C-2, 6), 146.0 (2C, galloyl C-3, 5), 140.1 (galloyl C-4), 116.9, 115.7, 114.3 (ter. C-1, 1′, 1″), 129.8, 124.5, 142.3 (ter. C-2, 2′, 2″), 110.1, 108.2, 139.7 (ter. C-3, 3′, 3″), 149.2, 145.4, 140.3 (ter. C-4, 4′, 4″), 137.7, 136.7, 139.2 (ter. C-5, 5′, 5″), 149.8, 144.8, 108.6 (ter. C-6, 6′, 6″), 169.8, 115.7 (che. C-1, 1′). 66.4, 118.5 (che. C-2, 2′), 41.1, 116.7 (che. C-3, 3′), 39.3, 146.6 (che. C-4, 4′), 30.4, 139.4, (che. C-5, 5′), 173.2, 140.9 (che. C-6, 6′), 165.4, 165.6, 166.2, 168.8, 169.8, 170.9, 173.2, 173.6 (–COO–).

Methylation of 15 A mixture of **15** (300 mg), dimethyl sulfate (3 ml) and anhydrous potassium carbonate (3.0 g) in dry acetone (25 ml) was treated as described for **14** to yield **15a** (95 mg) as an off-white amorphous powder, $[\alpha]_D^{16}$ $+23.6°$ ($c=1.0$, $CHCl_3$). FD-MS *m/z*: 1378 $[M^+]$. *Anal.* Calcd for $C_{65}H_{70}O_{33}$: C, 56.60; H, 5.12. Found: C, 56.79; H, 5.33. ^{1}H-NMR ($CDCl_3$) δ: 2.35 (1H, dd, $J=18$, 10 Hz, che. H-5), 2.70 (1H, d, $J=10$ Hz, che. OH), 2.96 (1H, dd, $J=18$, 5 Hz, che. H-5), 3.22, 3.42, 3.60, 3.64, 3.66, 3.72, 3.88, 3.89, 3.92, 3.94, 3.99 (each s, 51H in total, OMe), 4.39, 4.73, 5.07 (each 1H, t, $J=10$ Hz, H-5, 6), 4.83 (1H, t, $J=10$ Hz, che. H-2), 5.18 (1H, d, $J=10$ Hz, che. H-3), 5.37, 5.40 (each 1H, br s, H-2, 4), 5.80 (1H, br s, H-3), 6.74 (1H, br s, H-1), 6.71, 6.73, 7.20 (each 1H, s, aromatic H), 7.26 (2H, s, trimethoxybenzoyl H), 7.43 (1H, s, che. H-3′).

Alkaline Methanolysis of 15a A solution of **15a** (20 mg) in MeOH (2 ml) and 10% NaOH was heated under reflux for 1 h. Work-up as described for **13a** afforded **13c** (2.4 mg), **14b** (4.0 mg) and **15b** (8.4 mg). **15b**: a colorless syrup, $[\alpha]_D^{25}$ $+21.6°$ ($c=1.0$, $CHCl_3$). CD ($c=1.0\times10^{-2}$, MeOH) $[\theta]^{20}$ (nm): -78000 (228), $+78000$ (254), -14000 (315). ^{1}H-NMR ($CDCl_3$) δ: 3.38, 3.61, 3.62, 3.63, 3.76, 3.81, 3.88, 3.91, 3.93 (each s, 33H in total, OMe), 7.18, 7.34 7.39 (each 1H, s, aromatic H).

Partial Hydrolysis of 15 in Hot Water A solution of **15** (300 mg) in H_2O (3 ml) was heated at 95 °C for 30 h. Work-up as described for **14** afforded **7** (2.5 mg) and **15c** (4.5 mg). **15c**: an off-white amorphous powder, $[\alpha]_D^{15}$ $+3.0°$ ($c=0.6$, MeOH). Negative FAB-MS *m/z*: 1139 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{36}O_{33}\cdot 5H_2O$: C, 46.83; H, 3.77. Found: C, 47.09; H, 3.70. ^{1}H-NMR (acetone-d_6+D_2O) δ: 2.44 (1H, dd, $J=16$, 4 Hz, che. H-5), 3.00, (1H, d, $J=16$, 10 Hz, che. H-5), 4.25 (1H, d, $J=5$ Hz, H-2), 4.65 (1H, m, che. H-3), 5.01 (1H, d, $J=4$ Hz, H-4), 5.49 (1H, d, $J=2$ Hz, che. H-2), 5.70 (1H, d, $J=4$ Hz, H-3), 6.29 (1H, d, $J=5$ Hz, H-1), 6.80, 6.85, 6.93 (each 1H, s, aromatic H), 7.13 (1H, s, che. H-3′), 7.18 (2H, s, galloyl H).

Macarinin C (16) An off-white amorphous powder, $[\alpha]_D^{15}$ $-28.4°$ ($c=0.9$, MeOH). Negative FAB-MS *m/z*: 1103 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{32}O_{31}\cdot 5H_2O$: C, 48.25; H, 3.54. Found: C, 47.74; H, 3.47. ^{1}H-NMR (270 MHz, acetone-d_6+D_2O) δ: 2.18 (2H, m, che. H-5), 3.90 (1H, m, che. H-4), 4.51 (1H, dd, $J=8$, 6 Hz, H-6), 4.90—5.05 (2H, m, H-5, 6), 4.95 (1H, d, $J=8$ Hz, che. H-2), 5.13 (1H, d, $J=8$ Hz, che. H-3), 5.20 (1H, br s, H-4), 5.55 (1H, br s, H-2), 6.04 (1H, s-like, H-3), 6.58 (1H, br s, H-1), 6.82, 6.96, 7.32 (each 1H, s, aromatic H), 7.20 (2H, s, galloyl H), 7.53 (1H, s, che. H-3′). ^{13}C-NMR (acetone-d_6+D_2O) δ: 91.7 (glc C-1), 70.3 (glc C-2), 62.4 (glc C-3), 66.1 (glc C-4), 73.8 (glc C-5), 63.9 (glc C-6), 120.0 (galloyl C-1), 110.6 (2C, galloyl C-2, 6), 146.1 (2C, galloyl C-3, 5), 140.0 (galloyl C-4), 122.1, 114.2, 112.1 (ter. C-1, 1′, 1″), 130.7, 124.2, 140.8 (ter. C-2, 2′, 2″), 114.7, 107.6, 136.6 (ter. C-3, 3′, 3″), 148.5, 145.9, 143.9 (3C) (ter. C-4, 4′, 4″, 5, 5″), 136.4 (ter. C-5′), 145.3 (2C), 109.9 (ter. C-6, 6′, 6″), 169.8, 115.9 (che. C-1, 1′), 66.5, 118.7 (che. C-2, 2′), 41.1, 117.1 (che. C-3, 3′), 39.4,

146.4 (che. C-4, 4'), 30.1, 139.8 (che. C-5, 5'), 173.7, 141.0 (che. C-6, 6'), 163.4, 165.2, 165.6, 165.7, 168.5, 169.8, 173.1, 173.7 (–COO–).

Macaranin C (17) A yellow amorphous powder, $[\alpha]_D^{15}$ −45.6° (c=1.0, MeOH). Negative FAB-MS m/z: 1119 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{32}O_{32}\cdot 6H_2O$: C, 46.99; H, 3.62. Found: C, 46.71; H, 3.55. ^{1}H-NMR (acetone-d_6+D_2O) δ: 4.20—4.25 (1H, m, H-6), 4.60—4.90 (2H, m, H-5, 6), 4.94 (1/3H, d, J=2 Hz, DHHDP H-1), 5.16 (2/3H, s, DHHDP H-1), 5.30—5.60 (3H, m, H-2, 3, 4), 6.26 (1/3H, d, J=2 Hz, DHHDP H-3), 6.54 (2/3H, s, DHHDP H-3), 6.60 (1H, br s, H-1), 6.73, 7.05, 7.16, 7.26 (each 1H, s, aromatic H), 7.20 (2H, s, galloyl H). ^{13}C-NMR (acetone-d_6+D_2O) δ: 46.2, 52.0 (DHHDP C-1), 62.4, 63.3, 63.8, 64.1, 65.9, 66.8, 69.7, 72.7, 73.3 (glc C-2—6), 90.8, 91.9 (glc C-1), 92.4 (DHHDP C-6, 5), 96.2 (DHHDP C-5), 108.9, 109.0, 109.9, 110.7, 110.9, 112.4, 113.5, 115.8, 116.2, 117.0, 119.4, 120.2, 123.8, 124.8, 125.0, 128.7, (galloyl C-1; mac. C-1, 1', 1'', 2, 2', 3, 3', 6''; DHHDP C-1', 2', 3, 3', 6), 110.7, 110.9 (galloyl C-2, 6), 136.5, 137.5, 139.0, 140.1, 140.5, 141.2, 141.7, 143.4, 144.6, 145.6, 145.8, (galloyl C-4; mac. C-2'', 3'', 4, 4', 4'', 5, 5', 5'', 6, 6'; DHHDP C-4', 5', 6'), 149.1, 154.4 (DHHDP C-2), 146.0 (2C, galloyl C-3, 5), 164.9, 165.4, 165.6, 165.9, 167.8 (–COO–), 191.8, 194.5 (DHHDP C-4).

Preparation of the Phenazine Derivative (17a) A solution of **17** (50 mg) in EtOH (3 ml) was treated with *o*-phenylenediamine (10 mg) in 20% AcOH–EtOH (3 ml). The mixture was left standing at room temperature for 12 h. After concentration, the reaction mixture was chromatographed over MCI-gel CHP 20P (H_2O–MeOH) to afford **17a** (43 mg) as a tan amorphous powder, $[\alpha]_D^{15}$ +7.4° (c=0.7, MeOH). Negative FAB-MS m/z: 1173 $[M-H]^-$. *Anal.* Calcd for $C_{54}H_{34}N_2O_{29}\cdot 4H_2O$: C, 52.01; H, 3.40; N, 2.25. Found: C, 51.99; H, 3.47; N, 1.99. ^{1}H-NMR (acetone-d_6+D_2O) δ: 3.95—4.20 (1H, m, H-6), 4.70—5.04 (2H, m, H-5, 6), 5.23 (1H, d, J=4 Hz, H-3), 5.54 (1H, d, J=4 Hz, H-4), 5.69 (1H, d, J=5 Hz, H-2), 6.16 (1H, d, J=5 Hz, H-1), 6.79, 6.85, 7.16 (each 1H, s, mac. H), 7.00 (2H, s, galloyl H), 7.47 (1H, s, ph. H-3'), 7.97—8.36 (4H in total, m, ph. H-3'', 4'', 5'', 6''), 8.31 (1H, s, ph. H-3). ^{13}C-NMR (acetone-d_6+D_2O) δ: 65.2 (glc C-6), 67.6 (glc C-4), 68.6 (glc C-3), 76.6 (glc C-2), 77.1 (glc C-5), 91.7 (glc C-1), 108.9, 109.6, 111.8, 113.2, 115.0, 116.4, 117.0, 119.6, 120.2, 123.6, 124.4 (galloyl C-1; mac. C-1; 1', 1'', 2, 2', 3, 3', 6''; ph. C-1, 1', 2'), 110.2 (galloyl C-2, 6), 130.2, 132.4 (each 2C, ph. C-3'', 4'', 5'', 6''), 136.0, 137.1 137.6, 139.0, 139.5, 139.9, 140.6, 141.6, 142.7, 142.9 (2C), 145.2 (2C), 145.3 (2C), 146.4, 152.2 (galloyl C-4; mac. C-2'', 3'', 4, 4', 4'', 5, 5', 5'', 6, 6'; ph. C-1'', 2, 2'', 4, 4', 5, 5', 6, 6'), 146.0 (2C, galloyl C-3, 5), 165.1, 166.3, 166.5, 166.6, 168.1, 170.0 (–COO–).

Partial Hydrolysis of 17a in Hot Water A solution of **17a** (18 mg) in H_2O (2 ml) was heated at 90 °C for 2 h. After cooling, the precipitates formed were collected by filtration, and identified as **12b** by IR spectral comparison. The filtrate was purified by MCI-gel CHP 20P chromatography to afford **13** (4.5 mg).

Macarinin A (18) A yellow amorphous powder, $[\alpha]_D^{15}$ −42.0° (c=1.1, MeOH). Negative FAB-MS m/z: 1119 $[M-H]^-$. *Anal.* Calcd for $C_{48}H_{32}O_{32}\cdot 3H_2O$: C, 49.07; H, 3.26. Found: C, 49.25; H, 3.38. ^{1}H-NMR (acetone-d_6+D_2O) δ: 4.25—4.50 (1H, m, H-6), 4.60—4.90 (2H, m, H-5, 6), 4.94 (1/3H, d, J=2 Hz, DHHDP H-1), 5.17 (2/3H, s, DHHDP H-1), 5.35—5.60 (3H, m, H-2, 3, 4), 6.25 (1/3H, d, J=2 Hz, DHHDP H-3), 6.53 (2/3H, s, DHHDP H-3), 6.54 (1H, br s, H-1), 6.73, 7.01, 7.11, 7.19, 7.20, 7.26 (4H in total, each s, aromatic H), 7.21 (2H, s, galloyl H). ^{13}C-NMR (acetone-d_6) δ: 46.2, 52.1 (DHHDP C-1), 62.8, 63.7, 66.1, 66.9, 70.0, 70.7, 73.5 (glc C-2—6), 90.1, 92.0 (glc C-1), 92.4, 96.2 (DHHDP C-5, 6), 108.8 (2C), 109.0, 110.2, 113.4, 114.1 (2C), 115.3, 115.8, 117.1, 119.4, 120.2, 124.5, 124.8, 128.7, 130.2 (galloyl C-1; ter. C-1, 1', 1'', 2, 2', 3, 3', 6''; DHHDP C-1', 2', 3, 3', 6), 110.7 (2C, galloyl C-2, 6), 136.9, 137.4, 137.8, 138.9, 139.2, 139.8, 140.1, 140.6, 142.3, 143.3, 144.8 (2C), 145.5, 145.8, 147.7, 149.2, 149.8 (2C), 154.4 (galloyl C-4; ter. C-2'', 3'', 4, 4', 4'', 5, 5', 5'', 6, 6'; DHHDP C-2, 4', 5', 6'), 146.0 (2C, galloyl C-3, 5), 164.7, 165.3, 165.6, 166.0, 168.4, 170.4 (–COO–), 191.8, 194.5 (DHHDP C-4).

Preparation of the Phenazine Derivative (18a) A solution of **18** (205 mg) in EtOH (10 ml) was treated with *o*-phenylenediamine (28 mg) in 20% AcOH–EtOH (8 ml), and the mixture was left standing at room temperature for 10 h. Work-up as described above yielded **18a** (157 mg) as a tan amorphous powder, $[\alpha]_D^{15}$ −12.6° (c=0.7, MeOH). Negative FAB-MS m/z: 1173 $[M-H]^-$. *Anal.* Calcd for $C_{54}H_{34}N_2O_{29}\cdot 2H_2O$: C, 52.78; H, 3.28; N, 2.28. Found: C, 52.97; H, 3.33; N, 2.14. ^{1}H-NMR (acetone-d_6+D_2O) δ: 3.95—4.10 (1H, m, H-6), 4.70—5.00 (2H, m, H-5, 6), 5.42 (1H, d, J=4 Hz, H-3), 5.58 (1H, d, J=4 Hz, H-4), 5.67 (1H, d, J=6 Hz, H-2), 6.17 (1H, d, J=6 Hz, H-1), 6.77, 6.79, 6.96 (each 1H, s, ter. H), 6.99 (2H, s, galloyl H), 7.48 (1H, s, ph. H-3'), 7.90—8.40 (4H in total, m, ph. H-3'', 4'', 5'', 6''), 8.30 (1H, s, ph. H-3). ^{13}C-NMR (acetone-d_6+D_2O) δ: 65.1 (glc C-6), 67.8 (glc C-4), 68.6 (glc C-3), 76.6 (glc C-2), 77.1 (glc C-5), 91.6 (glc C-1), 108.5, 108.8, 110.5, 113.3, 114.7, 115.7, 116.5, 116.6, 117.1, 119.7, 119.9, 120.3, 124.4 (galloyl C-1; ter. C-1, 1', 1'', 2', 3, 3', 6''; ph. C-1, 1', 2', 3, 3'), 110.1 (2C, galloyl C-2, 6), 130.3 (ter. C-2), 130.1, 132.3 (each 2C, ph. C-3'', 4'', 5'', 6''), 136.0, 136.6, 137.7, 139.1, 139.4, 139.6, 139.7, 140.0, 140.2, 142.3, 142.8, 145.0, 145.3 (2C), 145.7, 149.7, 150.1, 152.2 (galloyl C-3, 4, 5; ter. C-3'', 4, 4', 4'', 5, 5', 5'', 6, 6'; ph. C-1'', 2, 2'', 3, 3', 4, 4', 5, 5', 6, 6'), 164.9, 166.1, 166.6, 167.9, 168.4, 171.1 (–COO–).

Partial Hydrolysis of 18a in Hot Water A solution of **18a** (50 mg) in H_2O (5 ml) was heated at 90 °C for 3.5 h. Work-up as described for **17a** gave **12b** (8 mg) and **7** (18 mg).

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14) Upfield shifts of the anomeric proton signal are often observed in phenazine derivatives, and this phenomenone may be interpreted in terms of conformational change of the glucopyranose ring, caused by aromatization of the hydrated cyclohexenetrione moiety, as well as the anisotropic effect of the *R*-oriented phenazine moiety.
15) The name, macaranic acid, is now proposed for this new phenolcarboxylic acid.
16) The lowfield shift of the H-6 signal can be well interpreted in terms of the anisotropic effect of the branched aromatic ring. When the branched aromatic ring is located at the aromatic ring linked to the glucose C-3 position, the distance between these protons and the aromatic ring is short.
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