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Constituents of *Geranium thunbergii* Sieb. et Zucc. IV.[1] Ellagitannins. (2). Structure of Geraniin[2]

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The main tannin of *Geranium thunbergii* has been isolated as yellow crystals, and named geraniin. Geraniin gave upon hydrolysis in boiling water, gallic acid, hexahydroxydiphenic acid, ellagic acid, and corilagin, and is shown by the proton nuclear magnetic resonance spectra to be a corilagin derivative esterified at O-2 and O-4 of D-glucopyranose in the molecule. Upon condensation with *o*-phenylenediamine, geraniin yielded a phenazine derivative, named phenazine A (X), which was transformed into phenazine B (XI) upon prolonged reaction. These two phenazine derivatives gave phenazine C (XII) by further prolonged reaction, or by hydrolysis of X or XI in boiling water. Corilagin was also isolated from the hydrolysis products mixture. The structure of phenazine C was proved by identification of its hydrolyzed product XV with synthetic specimen which was prepared *via* hydrogenolysis of dimethyl dimethoxytetrabenzyloxydiphenoate. These data along with the PMR spectra show that the structure of geraniin to be I. The carbon nuclear magnetic resonance spectra of geraniin indicate partial hydration to form geminal diol at the cyclohexenetrione moiety.

Keywords——dehydrohexahydroxydiphenoyl ester of corilagin; PMR and CMR spectra; hydrolysis; phenazine derivatives from geraniin; synthesis of phenazines; tannin structure determination

Preparation of a crude ellagitannin, temporarily named tannin 1, from the extract of *Geranium thunbergii* Sieb. et Zucc. was reported in Part II[4] of this series. Upon further purification, we have isolated a pure ellagitannin, named geraniin, which is regarded as the main tannin of this plant, and determined its structure to be I.

Geraniin, when repeatedly recrystallized from a mixture of MeOH and H_2O, formed yellow crystals, $C_{41}H_{28}O_{27}\cdot xH_2O$, $[\alpha]_D^{15}$ $-141°$ (hexahydrate, $c=0.5$, MeOH). A single spot was shown on paper-partition chromatography (PPC) and paper electrophoresis, and the characteristic color of ellagitannin[1,4] was given by the reaction with NO_2^-. The products of hydrolysis of tannin 1 in boiling water,[3] *i.e.*, gallic acid (II), ellagic acid (III), hexahydroxydiphenic acid (IV) and corilagin (V), were produced upon analogous hydrolysis of geraniin, and the products were fractionated by preparative thin-layer chromatography (prep. TLC) after methylation with diazomethane to give methyl tri-*O*-methylgallate (VI), tetra-*O*-methylellagic acid (VII), dimethyl hexamethoxydiphenoate (VIII), and nonamethylcorilagin (IX).[4] Proton nuclear magnetic resonance (PMR) spectrum of geraniin measured in acetone-d_6 (Table I) shows seven protons including that of anomeric proton of sugar, in the region of aromatic and vinyl protons, among which four protons can be regarded as due to the identical protons as the aromatic protons in corilagin.[5] Downfield shifts of H-2 and H-4 of glucopyranose to δ 5.4—5.6 ppm from those of corilagin (δ 4.06 and 4.42) are observed. A one-proton singlet is exhibited at δ 5.16. These spectral evidences along with

1) Part III: T. Okuda, K. Mori, and N. Hayashi, *Yakugaku Zasshi*, **96**, 1143 (1976).
2) A part of this work was presented at the 96th Annual Meeting of Pharmaceutical Society of Japan, Nagoya, April 1976. A preliminary paper has been published: T. Okuda, T. Yoshida, and H. Nayeshiro, *Tetrahedron Lett.*, **1976**, 3721.
3) Location: *1-1-1 Tsushima-naka, Okayama, 700, Japan.*
4) T. Okuda, T. Yoshida, and K. Mori, *Yakugaku Zasshi*, **95**, 1462 (1975).
5) T. Okuda, T. Yoshida, and K. Mori, *Phytochemistry*, **14**, 1877 (1975).

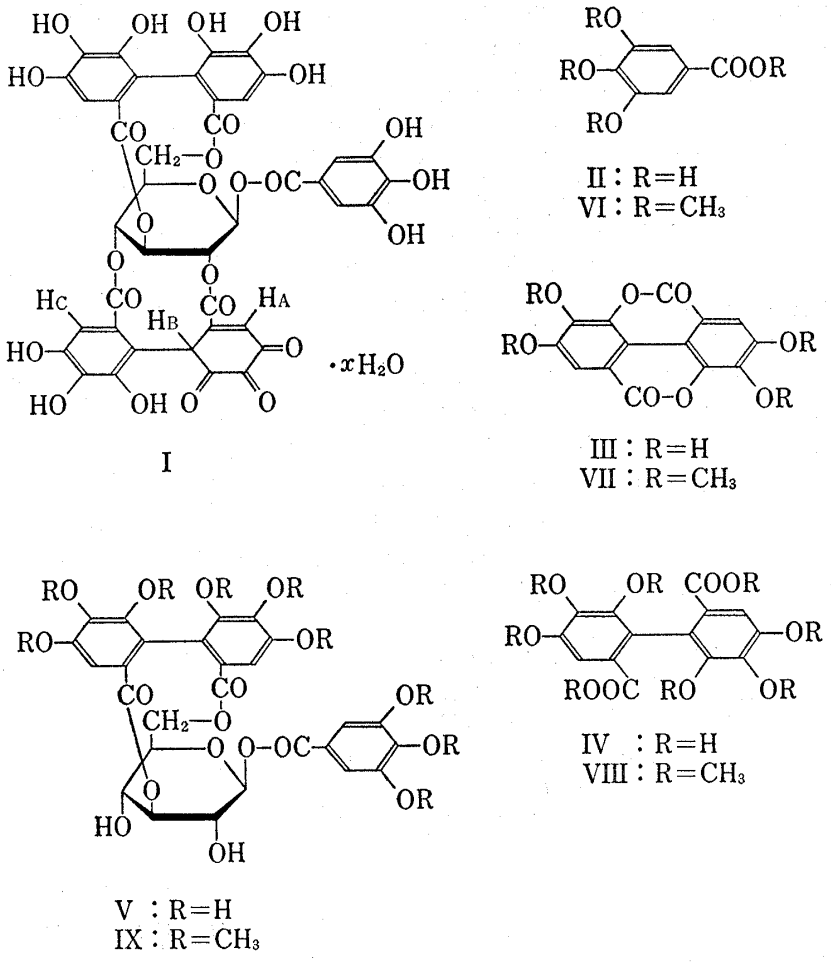


Chart 1

TABLE I. PMR Signals[a] of I, V, X and XI

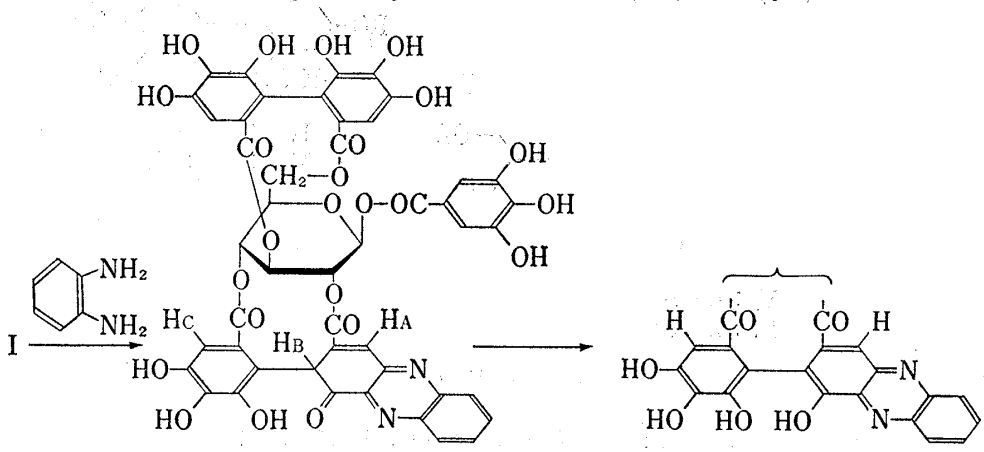
Compounds	Glucopyranose							Galloyl	Hexahydroxydiphenoyl		H_A	H_B	H_C
	H_1	H_2	H_3	H_4	H_5	H_6	$H_{6'}$						
V	6.35	4.06	4.83	4.42	4.54	5.00	4.08	7.09	6.67	6.81	—	—	—
I	6.55	≈5.60	≈5.00	≈5.60	4.28	≈5.60	≈5.00	7.20	6.67	7.13	6.53	5.16	7.21
X	6.62	5.56	≈4.64	≈5.46	4.39	≈5.76	≈4.64	7.19	6.67	7.06	7.07	5.33	7.33
XI	6.14	5.63	5.48	5.48	4.99	4.72	4.03	6.99	6.70	6.99	8.24	—	7.46

a) In acetone-d_6.

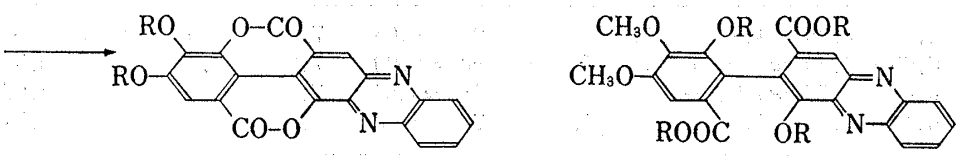
the results of hydrolysis show that geraniin is a derivative of V esterified at *O*-2 and *O*-4 of D-glucopyranose.

The solution of geraniin was turned red by phenylhydrazine–AcOH, and gave pale yellow precipitate upon the reaction with *o*-phenylenediamine solution in 15% AcOH at room temperature. This precipitate was purified by reprecipitation from MeOH–$CHCl_3$ to give amorphous powder, $C_{47}H_{30}N_2O_{24}\cdot 6H_2O$, (X), $[\alpha]_D^{15}$ −163° (*c*=0.5, MeOH), which was named phenazine A. Upon the reaction of geraniin with *o*-phenylenediamine in 50% AcOH, yellow precipitate was produced, and this product was purified by analogous reprecipitation to give amorphous powder, $C_{47}H_{30}N_2O_{24}\cdot 5H_2O$, (XI), $[\alpha]_D^{15}$ −90° (*c*=0.5, dioxane), which was named phenazine B. Phenazine B was also obtained when the reaction mixture producing X or an acetone solution of X was left stand or warmed. When aqueous solution of either X or XI was kept at boiling temperature for 1.5 hr, or the reaction mixture yielding phenazine B was

kept for longer time or at higher temperature, dark brown-red precipitate was produced, and was recrystallized from tetrahydrofuran to give needles of phenazine C, $C_{20}H_8N_2O_6 \cdot H_2O$, (XII), *m/e* 372 ($M^+$). The mother liquor of XII gave, upon evaporation followed by fractionation of methylated residue, VI, VII, VIII and IX. Phenazine C yielded dibenzoate, $C_{34}H_{16}N_2O_8$, diacetate, $C_{24}H_{12}N_2O_8$, and di-*O*-methyl derivative, XIII, $C_{22}H_{12}N_2O_6$, which yielded upon hydrolysis, hydroxy acid XIV. This acid was converted by the treatment with diazomethane, to dimethyl ester of tetra-*O*-methyl derivative, XV, $C_{26}H_{24}N_2O_8$, mp 130°. This ester was also produced upon the reaction of XIII with dimethyl sulfate in alkali, but the main product, XVI, $C_{27}H_{26}N_2O_8$, was found to have a C-methyl group (PMR, $CDCl_3$, δ 2.76) which is presumed to have replaced the hydrogen near a pyrazine nitrogen in XV (δ 8.75). These reaction sequences, the properties of the products, and the result of acid hydrolysis of geraniin, which yielded more than 1 mole equivalent of hexahydroxydiphenic acid, indicate structures of these esters to be XV and XVI, and determination of XV structure was accomplished by synthesis. As the synthesis of XV *via* acetate of tribenzylellagic acid[6] was retarded by extreme low yield of this compound from tetraacetylellagic acid, present synthesis was carried out as follows. Hydrogenolysis of dimethyl dimethoxytetrabenzyloxydiphenoate (XVII)[7] followed by methylation with diazomethane yielded, *via* XVIII, tri-

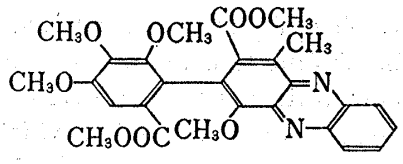


X XI



XII : R=H
XIII : R=CH_3

XIV : R=H
XV : R=CH_3



XVI

Chart 2

6) O. Th. Schmidt and G. Wieder, *Ann. Chem.*, **706**, 198 (1967).
7) O. Th. Schmidt, H. Voigt, W. Puff, and R. Koster, *Ann. Chem.*, **586**, 165 (1954).

benzyl derivative XIX, $C_{40}H_{38}O_{10}$, mp 146—147°, which was hydrogenolyzed to give XX, $C_{19}H_{20}O_{10}$, mp 152—154°. Oxidation of XX with *o*-chloranil yielded diketone XXI which was condensed with *o*-phenylenediamine to give XXII. Methylation of XXII with diazomethane gave XV. The production of XVIII by hydrogenolysis of XVII was accompanied by formation of a small amount of an isomer of XVIII. Comparisons of the properties of the product obtained by methylation of this isomer followed by hydrogenolysis, and those of XX, with the properties of XXIV which had been reported to be produced *via* XXIII,[6] support the assignments of structure XVIII to the main product of the hydrogenolysis of XVII, and structure XXIII to the isomeric minor product, although XV should be produced from either XVIII or XXIII.

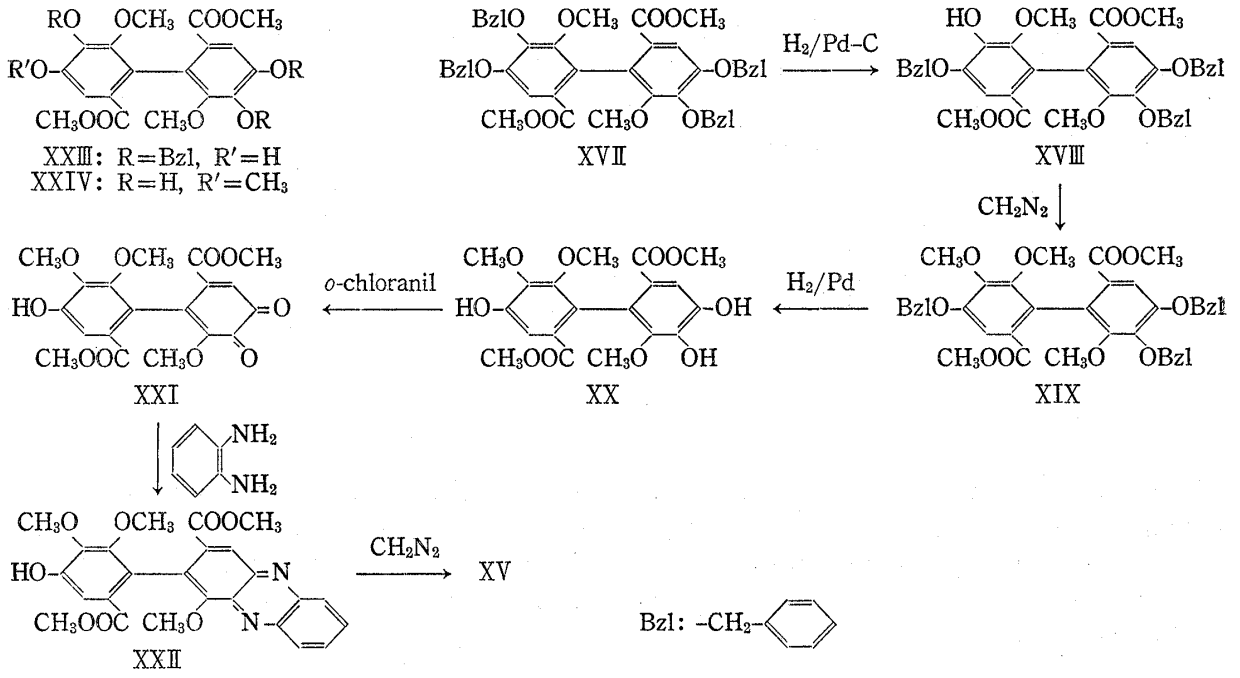


Chart 3

The process of phenazine C formation *via* phenazine A and phenazine B, and comparison of the signals in PMR spectra of these compounds, indicate structures X, XI and I for phenazine A, phenazine B and geraniin, respectively. The marked downfield shift of H_A in the PMR spectrum, upon the formation of XI (δ 8.24, s) from X (δ 7.07, d, J=2 Hz) is presumed to be due to aromatization of the ring, and the downfield shift of the same proton in X from that in geraniin (δ 6.53, s) would be the result of pyrazine ring formation. The decoupling experiment showed the allylic coupling between H_A and H_B (δ 5.53, d, J=2 Hz) in X, which is presumed to be due to conformational change occurred upon the production of X from geraniin.

As for the ester linkages at O-2 and O-4 of D-glucopyranose in geraniin, the one at O-2 rather than that at O-4, is presumed to be on the cyclohexenetrione moiety because of the significant upfield shift of the anomeric proton of D-glucopyranose from δ 6.55 to 6.14, upon the formation of XI from X, as this shift indicate nearby location of the phenazine ring.

The ^{13}C-NMR (CMR) spectra of geraniin generally show two peaks in the region of conjugated ketone, at δ 191—192 and at δ 194—195, and also peaks assignable to geminal diols at δ 91—97 alongside of C-1 signal of glucose, their shifts and patterns being varied depending on the water content and the solvent. These signals indicate geminal diol formation by partial hydration at cyclohexenetrione moiety of geraniin. The above mentioned shifts of ketone carbon peaks may occur either for conjugated ketone or for isolated ketone having geminal diols at α-carbon. The ketone group in phenazine A may also be hydrated to retard

enolization. Further investigations of hydration of cyclohexenetrione in geraniin molecule are in progress.

Geraniin was obtained in the yield of up to 1.6% from fresh plant collected in summer.[8] Comparison of this yield with the data of tannin analysis of the plant,[1] and the results of fractionation of the plant extract show that geraniin is the main tannin of *G. thunbergii*, and that appreciable parts of the phenolic compounds of smaller molecules reported previously[5,9] could be products of hydrolysis of geraniin occurred during extraction and fractionation. Among these phenolic compounds, brevifolin (XXV)[5] would presumably be decarboxylated product from brevifolin carboxylic acid (XXVI) which could be produced from the dehydrohexahydroxydiphenoyl residue upon the hydrolysis of geraniin. This presumption has been supported by combined gas chromatography–mass spectrometry (GC–MS) of methylated hydrolysis product of geraniin in boiling water, which showed presence of a product presumed to be XXVIII which is the fully methylated derivative of XXVI, based on the analogy of its fragmentation pattern to that of tri-*O*-methylbrevifolin (XXVII), in addition to M^+ ion (*m/e* 348) and $[M-COOMe]^+$ ion (*m/e* 289).

XXV: R=H
XXVII: R=CH_3

XXVI: R=H
XXVIII: R=CH_3

Chart 4

Crystalline geraniin shows almost no astringency on the tongue, and the weak astringency shown by its solution in aqueous ethanol is also incomparable to that of tannic acid of Japanese Pharmacopoeia, in spite of the appreciable astringency exhibited by geraniin when measured with hemoglobin.[1,4] Such properties of geraniin would have been favoring the medicinal application of *G. thunbergii*.

Experimental

Infrared (IR) spectra were recorded with JASCO IR-G, ultraviolet (UV) spectra were obtained with Shimadzu Double-40 Spectrophotometer, and $[\alpha]_D$ was measured with JASCO DIP-4 Digital Polarimeter. PMR spectra were recorded with Hitachi R-22 at 90 MHz with tetramethylsilane as internal standard, and CMR spectra were measured with NEVA's NV-21 at 22.6 MHz with ^2H internal lock and tetramethylsilane as the internal standard in acetone-d_6, tetrahydrofuran-d_8 and methanol-d_4. Gas liquid chromatography (GLC) was carried out with Shimadzu 5A gas chromatograph equipped with FID, using a glass column (2 m×3 cm i.d.) packed with 1% OV-1 on 80—100 mesh Chromosorb W, AW-HMDS, at column temperature 220°. MS were obtained with Shimadzu-LKB-9000 Gas Chromatograph–Mass Spectrometer by GC–MS or direct inlet system. Temperature of ion source 270°, ion accelerating voltage 3.5 kV, ionizing potential 70 eV, trap current 60 μA. Paper chromatography was performed on Toyo Filter Paper No. 50, and column chromatography was carried out on silica gel, Wako C-200. Paper electrophoresis was performed on Toyo Kagaku Sangyo PS-1510 at 600 V with 1% borax. Thin-layer chromatography (TLC) and prep. TLC were performed on Kieselgel PF_{254} (Merck). Solvents for TLC and prep. TLC: A, ligroin–$CHCl_3$–MeOH (7: 4: 1.5); B, benzene–$CHCl_3$–acetone (3: 1: 1); C, benzene–EtOAc (9: 1); D, $CHCl_3$–acetone (3: 1). Evaporation of solvents was carried out at the temperature lower than 40°.

Geraniin (I)——The crude ellagitannin temporarily named tannin 1[3] was recrystallized several times from MeOH–H_2O treating with activated charcoal to give yellow crystals. Seeding of MeOH–H_2O solution of the EtOAc extract from the aqueous acetone extract of the plant[3] with the crystals obtained above, after treating the EtOAc extract with ether and activated charcoal, yielded the same yellow crude crystals which were recrystallized from MeOH–H_2O to give geraniin, mp >360° (yield: 1.6% from fresh plant). PPC

8) The yield from dried herb described in the preliminary paper may be improved by proper treatment of the herb.

9) Y. Asahina and K. Tomimura, *Yakugaku Zasshi*, **38**, 405 (1918).

(colored with aq. $FeCl_3$ solution): *Rf* 0.41 (*n*-BuOH–AcOH–H_2O, 4: 1: 5, upper (BAW)); 0.18 (7% AcOH). $[\alpha]_D^{15}$ −141° (*c*=0.5, MeOH). UV λ_{max}^{MeOH} nm (log ε): 222 (4.74), 285 (4.45). IR ν_{max}^{KBr} cm^{-1}: 3400, 1735 (shoulder), 1730, 1710, 1700 (sh.), 1620, 1340, 1205. NMR (acetone-d_6) δ: 4.28 (m, 1H, glu-H_5), 4.67—5.00 (m, 2H, glu-H_3, H_6), 5.16 (s, 1H, H_B), 5.40—5.60 (m, 3H, glu-H_2, H_4, H_6), 6.53 (s, 1H, H_A), 6.55 (br. s, 1H, glu-H_1), 6.67 (s, 1H, hexahydroxydiphenoyl (HHDP)), 7.13 (s, 1H, HHDP), 7.20 (s, 2H, galloyl (gall.)), 7.21 (s, 1H, H_C). *Anal.* Calcd. for $C_{41}H_{28}O_{27}\cdot 5H_2O$: C, 47.22; H, 3.67. Found: C, 47.33; H, 3.57.[10]

Hydrolysis of Geraniin in Boiling Water——Geraniin (300 mg) in H_2O (150 ml) was refluxed in N_2 atmosphere for 1.5 hr, and H_2O was distilled *in vacuo*. The residue was dissolved in MeOH and treated with a solution of diazomethane in ether (CH_2N_2–ether). The solvent was distilled 12 hr later, and the CH_2N_2-treatment was repeated. After distilling the solvent, $CHCl_3$ was added to the residue, and insoluble material was recrystallized from pyridine to give pale yellow needles (40 mg) which were identified with tetra-*O*-methylellagic acid (VII) by IR spectra. The $CHCl_3$-soluble material was fractionated by prep. TLC (solvent A), and the constituent of *Rf* 0.50 was recrystallized from H_2O to give colorless needles, mp 83—84° (51.7 mg), which were identified with methyl tri-*O*-methylgallate (VI) by mixed mp and IR spectra. The fraction of *Rf* 0.42 gave pale yellow syrup (11 mg) which was identified with dimethyl hexamethoxydiphenoate (VIII) by GLC, MS and PMR. The fraction of *Rf* 0.30 showed upon GC–MS analysis, a GLC peak (t_R 8.5 min) which exhibited *m/e* 348 (M^+), 289 $(M-COOMe)^+$, 261, 247, 233, 219 and 212 ions. The fragment ions lower than 261 were almost identical with those of tri-*O*-methyl brevifolin (XXVII). The fraction of *Rf* 0.18 was recrystallized from MeOH to give colorless needles, mp 240—241°, which were identified with nona-*O*-methylcorilagin (IX) by mixed mp and IR spectra (35.6 mg).

Hydrolysis of Geraniin in 5% H_2SO_4——Geraniin (500 mg) in 5% H_2SO_4 (50 ml) was refluxed for 10 hr, precipitate was filtered and washed with H_2O. Recrystallization from pyridine yielded yellow needles (212 mg) which were identified as ellagic acid by IR spectra. The mother liquor was extracted with EtOAc (50 ml×3). The residue obtained by distillation of EtOAc solution was treated with CH_2N_2–ether for 5 hr, and after evaporation, the product was fractionated by prep. TLC (solvent A) to give the main product (*Rf* 0.50) which was extracted with $CHCl_3$ and recrystallized from H_2O to give colorless needles, mp 83—84° (90 mg), which were identified as methyl tri-*O*-methylgallate by mixed mp and IR spectra.

Phenazine A (X)——A solution of *o*-phenylenediamine (60 mg) in 15% AcOH (15 ml) was added to a solution of I (250 mg) in MeOH (5 ml), and the mixture was stirred for 30 min at room temperature. Pale yellow precipitate was filtered and washed with H_2O, and then reprecipitated from MeOH–$CHCl_3$ to give pale yellow amorphous powder (243 mg), mp >360°. PPC: *Rf* 0.48 (BAW, $FeCl_3$). λ_{max}^{MeOH} nm (log ε): 220 (4.93), 265 (4.73). ν_{max}^{KBr} cm^{-1}: 3380, 1730 (sh.), 1720, 1610, 1355, 1335, 1220. $[\alpha]_D^{15}$ −163° (*c*=0.5, MeOH). NMR (acetone-d_6) δ: 4.39 (m, 1H, glu-H_5), [4.64 (m, 2H), 5.46 (m, 1H), 5.76 (m, 1H)] (glu-H_3, H_4, H_6, $H_{6'}$), 5.33 (d, 1H, *J*=2 Hz, H_B), 5.56 (d, 1H, *J*=2 Hz, glu-H_2), 6.62 (d, 1H, *J*=2 Hz, glu-H_1), 6.67 (s, 1H), 7.06 (s, 1H) (HHDP), 7.07 (d, 1H, *J*=2 Hz, H_A), 7.19 (s, 2H, gall.), 7.33 (s, 1H, H_C), 7.78—8.22 (m, 4H, arom.). *Anal.* Calcd. for $C_{47}H_{30}N_2O_{24}\cdot 6H_2O$: C, 50.63; H, 3.79; N, 2.51. Found: C, 50.66; H, 3.75; N, 2.08.

Phenazine B (XI)——A solution of *o*-phenylenediamine (60 mg) in 50% AcOH (15 ml) was added to a solution of I (250 mg) in MeOH (5 ml), and the mixture was left stand for 5 hr. The solvent was distilled, and the residue was washed with H_2O, and reprecipitated from MeOH–$CHCl_3$ to give pale orange-yellow amorphous powder (250 mg), mp >360°. PPC: *Rf* 0.48 (BAW, $FeCl_3$). $[\alpha]_D^{15}$ −90° (*c*=0.5, dioxane). λ_{max}^{MeOH} nm (log ε): 220 (4.83), 280 (4.70). ν_{max}^{KBr} cm^{-1}: practically identical with the IR spectrum of X. NMR (acetone-d_6) δ: 4.03 (dd, 1H, *J*=4, 12 Hz, glu-$H_{6'}$), 4.72 (dd, 1H, *J*=8, 12 Hz, glu-H_6), 4.99 (dd, 1H, *J*=4, 8 Hz, glu-H_5), 5.48 (br. s, 2H, glu-H_3, H_4), 5.63 (d, 1H, *J*=6 Hz, glu-H_2), 6.14 (d, 1H, *J*=6 Hz, glu-H_1), 6.70 (s, 1H, HHDP), 6.99 (s, 3H, gall.-H×2, HHDP-H×1), 7.46 (s, 1H, H_C), 7.84—8.44 (m, 4H, arom.), 8.24 (s, 1H, H_A). *Anal.* Calcd. for $C_{47}H_{30}N_2O_{24}\cdot 5H_2O$: C, 51.47; H, 3.68; N, 2.55. Found: C, 51.65; H, 3.72; N, 2.27.

Phenazine C (XII)——The same reaction mixture as that afforded phenazine B by 5 hr reaction was left stand for 24 hr. The residue obtained by distilling solvent was treated with MeOH, and insoluble material was filtered and washed with H_2O. Recrystallization from tetrahydrofuran yielded dark brown-red needles, mp >360°. λ_{max}^{EtOH} nm (log ε): 282 (4.73), 335 (4.46), 405 (3.63). ν_{max}^{KBr} cm^{-1}: 3400, 1737, 1616, 1595, 1515, 1350, 1300, 1210. NMR (F_3CCOOD) δ: 8.06 (s, 1H), 8.26—8.89 (m, 4H), 9.61 (s, 1H). MS *m/e* 372 (M^+). *Anal.* Calcd. for $C_{20}H_8N_2O_6\cdot H_2O$: C, 61.55; H, 2.58; N, 7.18. Found: C, 61.16; H, 2.61; N, 6.92.

Upon acetylation of XII with Ac_2O–pyridine, a lemon-yellow amorphous diacetate, mp>360°, MS *m/e* 456 (M^+) was obtained. Benzoylation of XII with benzoyl chloride–dimethylformamide–pyridine yielded yellow amorphous dibenzoate, mp>360°, MS *m/e* 580 (M^+).

Hydrolysis of Phenazine A (X) and Phenazine B (XI)——Phenazine A or B (500 mg) in H_2O (500 ml) was refluxed in N_2 atmosphere for 1.5 hr. The precipitate from hot solution was filtered, washed with MeOH, and recrystallized from tetrahydrofuran to give dark brown-red needles which were identified with XII. The mother liquor and washing were combined, concentrated to dryness, and the residue was taken up in

10) The water content varied depending on the way of drying and storage. The sample for these data were dried *in vacuo* at 50°, over P_2O_5, and kept in a desiccator over silica gel at ordinary pressure for 3 days—1 week.

MeOH. The MeOH solution was treated with CH_2N_2–ether, and after evaporation of the solvent, the residue was fractionated by prep. TLC (solvent A). The fractionated products were identified with VI (82 mg), VIII (10.5 mg), IX (72.2 mg), and VII (70 mg), respectively.

Methyl 4-Methoxy-3-(4,5,6-trimethoxy-2-methoxycarbonylphenyl)phenazine-2-carboxylate (XV) from Phenazine C——Phenazine C (55 mg) was treated with excess CH_2N_2–ether twice for 12 hr each. The resulting dark brown precipitate was filtered, washed with MeOH, and reprecipitated from dimethylformamide to give dark brown amorphous powder (XIII), mp >360°, MS *m/e* 400 (M^+). This powder was dissolved in warm 10% NaOH (5 ml), and after cooling, H_2O (20 ml) was added. The resulting solution was neutralized with conc. HCl (0°) under ice-cooling to give orange-red precipitate which was filtered, washed with H_2O, and treated with CH_2N_2–ether for 12 hr after dissolving in MeOH (5 ml). The solvent was distilled and the residue which showed two spots (*Rf* 0.57, 0.55) on TLC (solvent B) was fractionated by prep. TLC (solvent B) to give the main product, *Rf* 0.55 (XV). Recrystallization from MeOH–H_2O gave yellow needles, mp 130—131°, yield 28 mg (38.5%). λ_{max}^{MeOH} nm (log ε): 267 (4.79), 370 (3.84). ν_{max}^{KBr} cm^{-1}: 2950, 1727, 1710, 1330, 1238, 1213, 1092. NMR ($CDCl_3$) δ: 3.56, 3.67, 3.77, 3.99, 4.00, 4.02 (OMe×6), 7.48 (s, 1H), 7.75—8.44 (m, 4H), 8.75 (s, 1H). MS *m/e* 492 (M^+). *Anal.* Calcd. for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.46; H, 5.18; N, 5.54.

The Product Having C-methyl Group (XVI)——To a solution of dimethyl ether (XIII) (70 mg) in 20% NaOH (2 ml) was added dimethyl sulfate (1 ml), and the solution was refluxed for 1 hr. 10% NaOH (10 ml) was added, and refluxing was continued for additional 2 hr. After cooling, the reaction mixture was neutralized with 10% HCl, precipitate was filtered, and washed with H_2O. The precipitate was dissolved in MeOH (10 ml) and treated with excess CH_2N_2–ether for 12 hr, and after distilling solvent, the product was fractionated by prep. TLC (solvent B) to give the constituent of *Rf* 0.57, which was recrystallized from MeOH–H_2O to afford yellow needles (XVI), mp 150—151°, yield 20 mg (21%). λ_{max}^{MeOH} nm (log ε): 265 (4.88), 368 (4.05). ν_{max}^{KBr} cm^{-1}: 2900, 1730, 1715, 1360, 1255, 1200, 1110. NMR ($CDCl_3$) δ: 2.76 (s, 3H, Me), 3.56 (MeO), 3.58 (MeO), 3.73 (MeO), 3.98 (MeO×2), 4.07 (MeO), 7.44 (s, 1H), 7.78—8.35 (m, 4H). MS *m/e* 506 (M^+). *Anal.* Calcd. for $C_{27}H_{26}N_2O_8$: C, 64.03; H, 5.17; N, 5.53. Found: C, 63.77; H, 5.25; N, 5.08.

Debenzylation of Dimethyl Dimethoxytetrabenzyloxydiphenoate (XVII)——Hydrogenolysis of XVII (2.0 g) in AcOH (200 ml) over 10% Pd-C was carried out to absorb 1 mol equivalent of H_2 (60 ml). After removing the catalyst and the solvent, the residue was dissolved in $CHCl_3$, and chromatographed on a silica gel column (3×30 cm) eluting with $CHCl_3$ to give colorless syrup (XVIII) from fractions No. 20—25 (5 ml portions), yield 516 mg (25.8%). TLC: *Rf* 0.54 (solvent C). NMR ($CDCl_3$) δ: 3.51, 3.53, 3.58, 3.61 (MeO×4), 5.14 (s, 4H, $C_6H_5C\underline{H}_2$-×2), 5.19 (s, 2H, $C_6H_5C\underline{H}_2$–), 5.91 (br. s, 1H, O$\underline{H}$), 7.25—7.51 (m, 17H). Fractions No. 26—28 yielded a colorless syrup (XXIII), yield 200 mg (10%). TLC: *Rf* 0.52. NMR ($CDCl_3$) δ: 3.49, 3.52, 3.55, 3.59 (MeO×4), 5.12 (s, 4H, $C_6H_5C\underline{H}_2$-×2), 5.17 (s, 2H, $C_6H_5C\underline{H}_2$–), 7.22—7.49 (m, 17H).

Methylation of Dimethyl Dimethoxytribenzyloxydiphenoate (XVIII)——Excess CH_2N_2–ether was added to a solution of XVIII (300 mg), and solvent was distilled 12 hr later. The residue was fractionated by prep. TLC (solvent C) to give the main product (*Rf* 0.65) which was extracted with $CHCl_3$ and recrystallized from MeOH to give colorless prisms (XIX), mp 146—147°, yield 214.4 mg (70%). ν_{max}^{KBr} cm^{-1}: 2940, 1727, 1590, 1326, 1200 (broad), 1090. NMR ($CDCl_3$) δ: 3.53, 3.55, 3.57, 3.60, 3.92 (MeO×5), 5.14 (s, 4H, $C_6H_5C\underline{H}_2$-×2), 5.18 (s, 2H, $C_6H_5C\underline{H}_2$–), 7.24—7.48 (m, 17H). *Anal.* Calcd. for $C_{40}H_{38}O_{10}$: C, 70.79; H, 5.64. Found: C, 70.65; H, 5.61.

Hydrogenolysis of Dimethyl Trimethoxytribenzyloxydiphenoate (XIX)——Hydrogenolysis of XIX (300 mg) was carried out in AcOH (100 ml) over Pd which had been activated by hydrogenation of $PdCl_2$ (50 mg) in MeOH (100 ml). The catalyst and the solvent were removed when absorption of H_2 ceased, and the residue was recrystallized from H_2O to yield colorless prisms (XX), mp 152—154°, yield 100 mg (56%). ν_{max}^{KBr} cm^{-1}: 3300, 1680, 1590, 1340, 1315, 1245 (broad), 1067, 1017. NMR (CD_3OD) δ: 3.43 (MeO), 3.54 (MeO×3), 3.89 (MeO), 7.25 (s, 1H), 7.30 (s, 1H). *Anal.* Calcd. for $C_{19}H_{20}O_{10}$: C, 55.88; H, 4.94. Found: C, 55.08; H, 4.95, 4.90. The carbon value was not raised by repeated experiments. However, structure XX was supported by production of VIII upon the treatment with CH_2N_2–ether.

Oxidation of Dimethyl Trimethoxytrihydroxydiphenoate (XX) and Condensation of the Product with *o*-Phenylenediamine——A solution of *o*-chloranil (30 mg) in dioxane (0.5 ml) was added to a solution of XX (50 mg) in dioxane (1 ml), and the mixture was stirred for 1 hr at room temperature. Petroleum ether was added to deposit red oil, and the upper layer was removed by decantation. The oil was reprecipitated from ether–petr. ether repeatedly to give a viscous oil (XXI), which was dissolved in ether (2 ml), and a solution of *o*-phenylenediamine (13.5 mg) in ether (2 ml) and a few drops of AcOH were added. The mixture was left stand at room temperature for 18 hr. The solvent was distilled, and the residue was fractionated by prep. TLC (solvent D), upon which the yellow zone of *Rf* 0.5 afforded by extraction with $CHCl_3$ a yellow syrup (XXII), yield 15 mg (25.6%). NMR (acetone-d_6) δ: 3.49, 3.59, 3.71, 3.92, 4.04 (MeO×5), 7.46 (s, 1H), 7.93—8.37 (m, 4H), 8.59 (s, 1H).

Methyl 4-Methoxy-3-(4,5,6-trimethoxy-2-methoxycarbonylphenyl)phenazine-2-carboxylate by Methylation of XXII——Excess CH_2N_2–ether was added to a solution of XXII (25 mg) in MeOH. The solvent was distilled 12 hr later, and the residue was fractionated by prep. TLC extracting with $CHCl_3$ to give the product of *Rf* 0.52, which was recrystallized from MeOH–H_2O to afford yellow needles, mp 160—161°, yield

21 mg (81.6%). When recrystallized from the solvent seeding with XV prepared from I, needles, mp 130—131°, were obtained, which were identified with XV by mixed mp and spectra. *Anal.* Calcd. for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.45; H, 4.93; N, 5.52.

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