Tannins and Related Compounds. CXVI.[1] Six New Complex Tannins, Guajavins, Psidinins and Psiguavin from the Bark of *Psidium guajava* L.

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Six new complex tannins, guajavins A (5) and B (1), psidinins A (9), B (11) and C (13), and psiguavin (15), together with a variety of condensed, hydrolyzable and complex tannins, have been isolated from the bark of *Psidium guajava* L. (Myrtaceae). On the basis of chemical and spectroscopic evidence, the structures of guajavins and psidinins were established to consist of a (+)-gallocatechin unit and a hydrolyzable tannin moiety linked *C*-glycosidically, while psiguavin was found to be a novel metabolite probably derived from eugenigrandin A (7) through successive oxidation, benzylic acid-type rearrangement, decarboxylation and oxidative coupling of the gallocatechin B-ring and one of the aromatic rings in the hydrolyzable tannin moiety.

Keywords *Psidium guajava*; Myrtaceae; complex tannin; guajavin; psidinin; psiguavin; *C*-glycosidic tannin; hydrolyzable tannin; flavan-3-ol; tannin

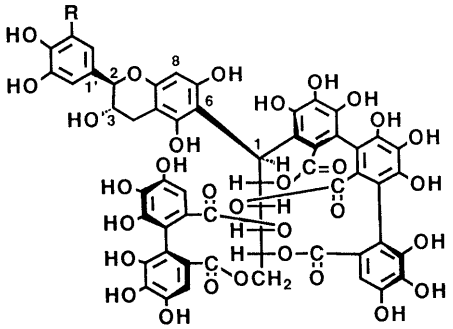
Most of the species of the large tropical and subtropical family, Myrtaceae, particularly of the genera *Eucalyptus*, *Eugenia*, *Syzygium* and *Psidium*, are known to be rich sources of tannins, and some of them have already been examined chemically.[2,3] In continuation of our studies on tannins in this family, we have now investigated the bark of *Psidium guajava* L. (Japanese name: banjiro), which is a native of tropical America and is now cultivated widely in the tropics for its edible fruits and also for medicinal purposes to treat diabetes, diarrhea and stomachache.[4] As a result, we have isolated, together with a variety of known condensed, hydrolyzable and complex tannins, six new complex tannins named guajavins A (**5**) and B (**1**), psidinins A (**9**), B (**11**) and C (**13**), and psiguavin (**15**), all consisting of a flavan-3-ol unit and a *C*-glycosidic ellagitannin moiety. This paper describes the isolation and structure elucidation of these compounds.

Repeated chromatography of the aqueous acetone extract over Sephadex LH-20 and reverse-phase gels (MCI-gel CHP 20P, Fuji-gel ODS G3 and Bondapak C_{18}/Porasil B) yielded twenty-two tannins and related compounds. Among them, four were found to be identical with the simple flavan-3-ols [(+)-catechin and (+)-gallocatechin (**3**)] and the proanthocyanidins (procyanidin B-1[5] and prodelphinidin B-1[6]), while eight were identified as the gallotannin [3,4,5-trimethoxyphenol 1-*O*-β-D-(2′,6′-di-*O*-galloyl)-glucopyranoside[7]], ellagitannins [2,3-(*S*)-hexahydroxydiphenoyl (HHDP)-6-*O*-galloyl-D-glucopyranose[8] and pedunculagin[9]] based on a glucopyranose core, and *C*-glycosidic ellagitannins (castalagin,[3,10] casuarinin,[10,11] valolaginic acid,[12] vescalagin carboxylic acid[13] and grandinin).[14] It should be noted here that the *C*-glycosidic ellagitannins are much more abundant in both qualitative and quantitative senses than their biogenetic precursors of ellagitannins possessing a glucopyranose core (see Experimental). This fact indicated that *C*-glycosidation readily occurs in this plant after formation of the HHDP group(s) on the glucopyranose ring. The complex tannins were readily characterized by their positive colorations with both the anisaldehyde–sulfuric acid reagent (pink)[15] and the nitrous acid test (brown),[16] and four were found to be identical with acutissimins A (**8**) and B (**2**),[17] eugenigrandin A (**7**)[18] and mongolicain A (**10**)[19] by comparisons of their physical and spectral data with those of authentic specimens.

The new complex tannin, guajavin B (**1**), showed, in the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, aliphatic signals at δ 4.40 (1H, d, J=4 Hz), 4.08 (1H, m) and 2.5—2.8 (2H, m), characteristic of the C-ring protons of the 2,3-*trans* flavan-3-ol.[17] The observation of one aromatic singlet at δ 6.11, the chemical shift being consistent with the phloroglucinol-type A-ring signals, indicated the presence of a substituent at the C-6 or C-8 position of the flavan nucleus, whereas a two-proton singlet at δ 6.54 assignable to the flavan B-ring protons implied the occurrence of a gallocatechin moiety. In addition, the spectrum exhibited three one-proton aromatic singlets at δ 6.64, 6.79 and 7.10. Since these aromatic singlets were considered to be assignable to the HHDP and/or nonahydroxytriphenoyl protons, the appearance of three signals suggested **1** to be *C*-glycosidic. Comparison of the ^{1}H-NMR spectrum of **1** with those of the known complex tannins showed that the chemical shifts and coupling patterns are almost the same as those of **2**, except for the two-proton aromatic singlet at δ 6.54. These ^{1}H-NMR observations suggested that the gallocatechin unit is linked to the *C*-glycosidic ellagitannin moiety through a carbon–carbon bond at the C-6 or C-8 position. This was also supported by negative fast atom bombardment mass spectrometry (FAB-MS), which exhibited the prominent $(M-H)^-$ peak at m/z 1221, 16 mass units more than that of **2**.

Ordinary phenol methylation of **1** afforded the eicosamethyl ether [field desorption mass spectrum (FD-MS) m/z: 1502 $(M)^+$]. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of the methylate showed a doublet signal (in the off-resonance experiment) at δ 96.8 arising from the flavan A-ring, whose chemical shift was closely correlated with that of the C-6 substituted flavan-3-ols (*e.g.* gambiriin A_3 nonamethyl ether; δ 96.1[20]) rather than the C-8 substituted alternatives (*e.g.* gambiriin A_1 nonamethyl ether; δ 88.6).[20] This fact clearly indicated that the hydrolyzable tannin moiety is linked at the C-6 position of the gallocatechin moiety.

To elucidate the structure of **1** more definitively, we attempted the synthesis[20-22] of **1** by condensation of (+)-gallocatechin (**3**) and vescalagin (**4**).[3,10] Namely, refluxing of a mixture of **3** and **4** in dry dioxane in the



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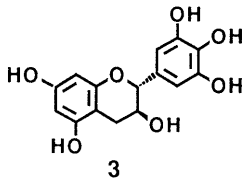
2: R=H



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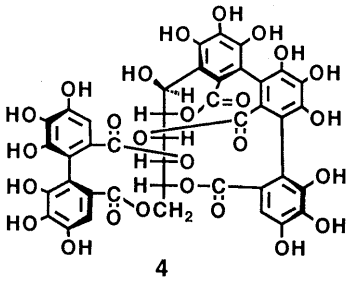

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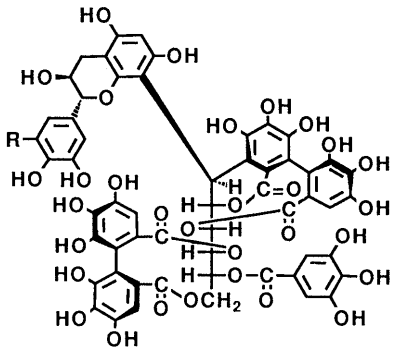
presence of *p*-toluenesulfonic acid yielded **1**, together with the C-8 substituted positional isomer, eugenigrandin A (**7**) in relatively high yields. Therefore, the structure of guajavin B was determined unequivocally to be as represented by the formula **1**.

The ^{1}H-NMR spectrum of guajavin A (**5**), measured at room temperature, was extremely complicated by conformational isomerism, which was commonly observed in the complex tannins having a substituent at the C-8 position of the flavan nucleus.[17,21,22] The ^{13}C-NMR spectrum, although similarly complicated, exhibited the galloyl C-2 and C-6 signals at δ 110.1 and the flavan C-2′ and C-6′ signals at δ 107.6, the latter suggesting the presence of a gallocatechin unit. The fact that the negative FAB-MS displayed the $(M-H)^-$ peak at *m/z* 1223, which was 2 mass units more than that of **1**, suggested the existence of a biphenyl and a galloyl group instead of the triphenoyl group. Actually, comparison of the ^{13}C-NMR spectrum with that of stenophyllanin A (**6**)[21] showed a close resemblance, except for the flavan B-ring signals.

Further confirmation of the location of the hydrolyzable tannin moiety at the flavan C-8 position was obtained by analysis of the ^{13}C-NMR spectrum of the eicosamethyl ether [FD-MS *m/z*: 1504 $(M)^+$], which showed a signal at δ 89.0 (d) arising from the A-ring, similar to that (δ 88.6) of the above-mentioned gambiriin A_1 methyl ether.[20] Finally, the structure of **5** was established by similar condensation of **3** and stachyurin,[10,11] thus permitting the assignment of the structure (**5**) for guajavin A.

The ^{1}H- and ^{13}C-NMR spectra of psidinins A (**9**), B (**11**) and C (**13**) were closely correlated with each other. Namely, these ^{1}H-NMR spectra characteristically showed a very sharp singlet at δ 4.37, 4.39 and 4.36, respectively, due to an isolated methine, in addition to signals of 2,3-*trans* flavan-3-ol and *C*-glycosidic ellagitannin moieties. In each case, a two-proton aromatic singlet assignable to the flavan B-ring protons appeared at δ 6.24, 6.51 and 6.42, suggesting the presence of a gallocatechin unit. The ^{13}C-NMR spectra exhibited signals due to a carbonyl group, a tetra-substituted olefine, an oxygen-bearing quaternary carbon and an aliphatic methine, the chemical shifts being in good agreement with those of the cyclopentenone part of mongolicains A (**10**) and B (**12**)[19] (Table I).

In the ^{1}H-NMR spectra of **9** and **11**, the flavan H-2 signals were observed at δ 5.37 (d, $J=3$ Hz)[23] and 4.64 (d, $J=8$ Hz), respectively, the former being shifted significantly downfield as compared with that of (+)-gallocatechin (**3**) (δ 4.48). This fact indicated that there is a through-



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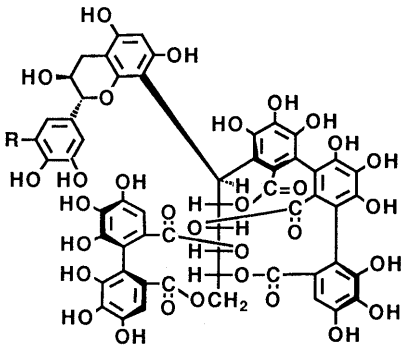
6: R=H



7: R=OH
8: R=H

space interaction between the H-2 signal and the A-ring substituent (the hydrolyzable tannin moiety) in **9**, and that the substituent is therefore located at the flavan C-8 position. On comparison of the ^{1}H-NMR spectra, the chemical shifts and coupling patterns in **9** and **11** were almost the same as those of mongolicains A (**10**) and B (**12**), respectively, except for the flavan B-ring signals. These findings, coupled with the observation of the same $(M-H)^-$ peak at *m/z* 1191 (16 mass units more than those of **10** and **12**) in the negative FAB-MS, indicated that **9** and **11** differ from **10** and **12**, respectively, only in the structure of the flavan-3-ol unit, which possesses a gallocatechin moiety.

Methylation of **9** yielded the heptadecamethyl ether, and subsequent alkaline methanolysis gave, among many uncharacterized products, dimethyl 3,3′,4,4′,5,5′-hexamethoxydiphenoate, the negative specific optical rotation [$-27.0°$ ($CHCl_3$)] thus confirming unambiguously that the chirality of the biphenyl bond is in the *S*-series.[24] On the other hand, in the case of **11**, methylation-

TABLE I. ^{13}C-NMR Spectral Data for Compounds **1**, **5**, **6**, **9**—**13** and **15** (δ-Values)[a]

	1	5	9	11	13	15	10	12	6
Glucose									
C-1	38.0	38.4	47.6	48.1	46.2	35.1	47.4	48.1	46.4
C-2	78.2	81.2	77.7	76.8	81.1	79.4	77.9	76.8	81.4
C-3	71.9	74.7	72.4	71.9	76.4	74.4	72.4	72.0	75.6
C-4	70.3	70.8	68.4	68.4	70.1	68.9	68.4	68.4	71.6
C-5	71.3	73.2	71.1	71.0	72.0	71.3	71.1	71.0	71.6
C-6	65.8	64.6	65.0	65.1	64.5	63.9	65.0	65.1	64.5
Flavan-3-ol									
C-2	82.5	82.2	79.6	82.7	81.1	80.1	79.9	82.7	81.7
C-3	68.3	68.0	66.9	67.1	67.6	67.4	67.0	67.2	66.9
C-4	29.4	31.5	24.0	30.4	27.5	29.8	24.3	27.6	27.8
C-4a	101.2	100.5	101.0	96.4	101.6	103.6	101.0	96.5	102.6
C-5	155.0	155.4	158.5	157.4	158.4	156.6	158.6	157.5	158.4
C-6	107.4	96.5	90.5	104.4	90.7	98.6	90.6	104.5	90.6
C-7	156.3	155.4	160.0	159.4	160.1	155.7	160.1	159.5	159.8
C-8	96.2	105.1	103.5	97.2	104.9	101.4	103.6	97.2	104.4
C-8a	155.0	155.4	151.6	153.6	151.7	154.2	151.6	153.6	151.9
C-1′	130.9	131.0	130.2	130.7	130.8		130.6	131.3	130.8
C-2′	107.5	107.6	105.0	107.3	106.1		113.2	115.2	115.0
C-3′	146.1	145.9	146.3	146.2	146.4		—	—	—
C-4′	133.4	133.0	132.7	133.4	133.1		—	—	—
C-5′	146.1	145.9	146.3	146.2	146.4		116.1	115.9	116.2
C-6′	107.5	107.6	105.0	107.3	106.1		117.6	119.8	121.3
Cyclopentenone									
C-1			50.3	50.7	49.6	143.6	50.3	50.7	49.6
C-2			140.6	140.3	139.4	48.6	140.1	140.1	137.5
C-3			148.9	149.2	149.3	91.8	148.9	149.2	149.6
C-4			197.2	196.9	195.7	198.0	196.9	196.8	196.1
C-5			89.2	89.3	90.7	150.6	89.3	89.3	90.2
C-1′						130.8			
C-2′						198.5			
C-3′						79.8			
C-4′						61.7			
C-5′						171.5			
Galloyl									
C-1		120.6			120.8				120.6
C-2		110.1			110.3				110.2
C-3		145.9			146.4				146.4
C-4		139.4			139.4				139.5
–COO–									
	167.1	168.2	168.2	168.2	165.5	164.1	163.6	163.8	166.3
	165.9	169.1	163.6	163.9	168.0	168.3	166.7	167.0	166.4
	167.3	168.4	166.8	167.1	167.0	168.0	167.3	167.0	167.8
	167.3	166.3	167.3	167.3	165.5	168.5	168.1	169.0	168.9
	169.3	169.5	169.5	169.4	169.0	168.6	169.4	169.3	169.3
						171.5			

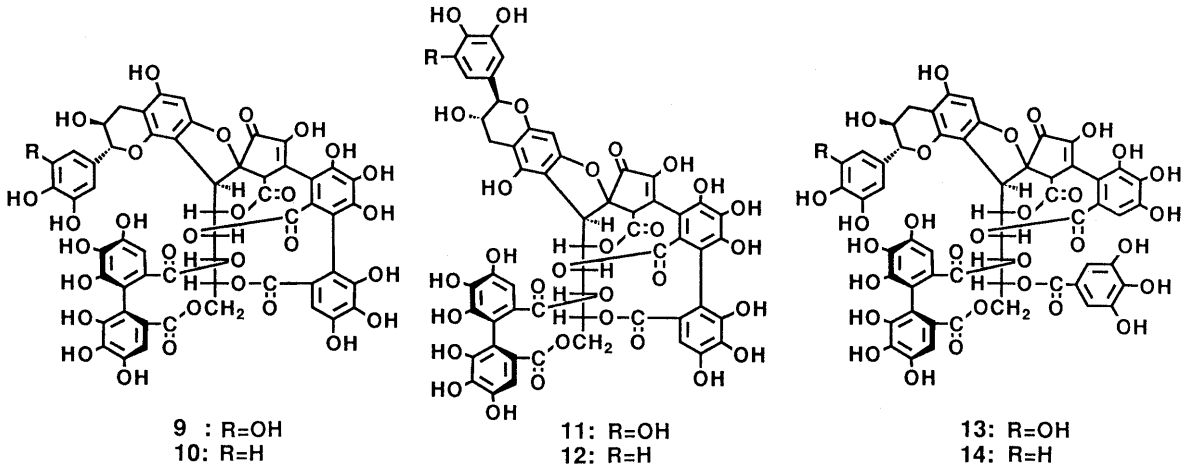
a) Measured at 25.05 MHz in acetone-d_6 + D_2O.

methanolysis studies could not be done owing to the lack of the sample, but considering the similarity of the ^{1}H-NMR spectra of **11** and **12**, the HHDP group was inferred to have the same *S*-absolute configuration.

Based on the findings mentioned above, the structures of psidinins A and B were concluded to be as shown by the formulae **9** and **11**, respectively.

The ^{1}H-NMR spectrum of **13** showed the presence of a galloyl group (δ 7.06, 2H, s), together with three one-proton aromatic singlets (δ 6.51, 6.63 and 7.00), suggesting that **13** is a stenophyllinin-type complex tannin.[25] The fact that the flavan H-2 signal appeared at δ 5.19 (d, J=6 Hz), which showed a shift similar to that of **9**, indicated that the *C*-glycosidic ellagitannin moiety is located at the C-8 position. Comparison of the ^{1}H- and ^{13}C-NMR spectra (Table I) with those of stenophyllinin A (**14**)[25] showed an extremely close resemblance in both aliphatic and aromatic fields, in addition to the presence of a gallocatechin unit in place of catechin. The negative FAB-MS [m/z 1193 $(M-H)^-$] of **13** also supported the presence of one extra oxygen atom as compared with that of **14**. On the basis of these findings, psidinin C was concluded to have the structure (**13**).

The ^{1}H-NMR spectrum of psiguavin (**15**) exhibited three sharp singlets at δ 6.72, 6.73 and 7.00 due to isolated aromatic protons. The signals at δ 6.28 (1H, s), 3.00 (1H, dd, J=7, 17 Hz) and 2.57 (1H, dd, J=8, 17 Hz) suggested the presence of the flavan A- and C-rings. In addition, signals arising from the polyalcohol moiety, assigned by proton–proton shift correlation spectroscopy (^{1}H–^{1}H COSY), were quite consistent with the *C*-glycosidic ellagitannin. In particular, the coupling manners of each signal were almost the same as those found in psidinin A (**9**), indicating that the modes of linkage of each acyl



9 : R=OH
10: R=H

11: R=OH
12: R=H

13: R=OH
14: R=H

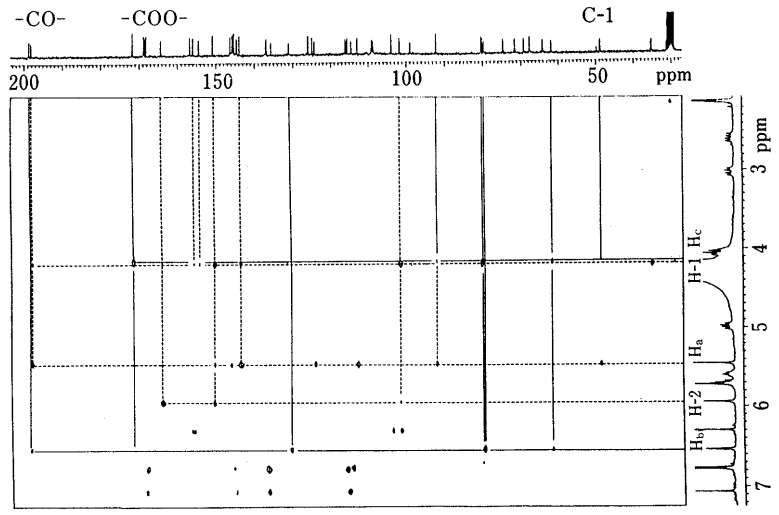
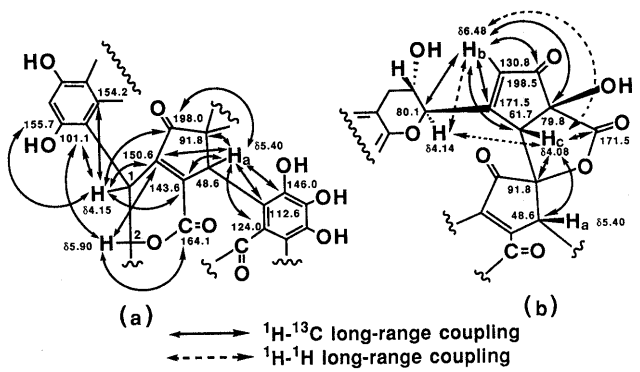
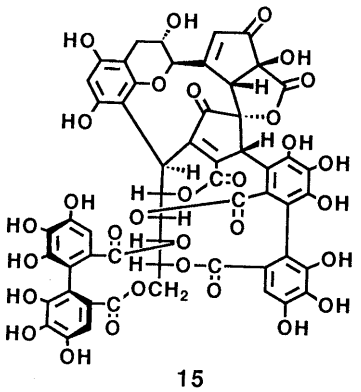


Fig. 1. ^{1}H–^{13}C Long-Range COSY Spectrum of Psiguavin (**15**)
$J = 10$ Hz, acetone-d_6 + D_2O.





15

Fig. 2. Partial Structures (a) and (b) of Psiguavin (**15**)

group are similar to those of **9**. In the proton–carbon long-range shift correlation (^{1}H–^{13}C long-range COSY) spectrum (Fig. 1), the polyalcohol H-1 signal (δ 4.15, s) was found to be correlated with the flavan A-ring signals at δ 101.4, 154.2 and 155.7, thus confirming that the polyalcohol C-1 is connected to the flavan A-ring through a carbon–carbon linkage. Furthermore, this H-1 signal showed cross peaks with olefinic carbon signals at δ 150.0 and 143.6 and a carbonyl signal at δ 196.9. Since the polyalcohol H-2 signal (δ 5.90, s) was found to be correlated with one (δ 150.0) of the olefinic signals, the polyalcohol C-1 was proved to be bonded to the olefinic carbon. On the other hand, the benzylic methine (H_a) signal (δ 5.40, s) showed, together with cross peaks with the signals of the oxygen-bearing quaternary carbon (δ 91.8) and aromatic carbons, correlations with the above-mentioned carbonyl (δ 196.9) and olefinic carbons (δ 150.0 and 143.6). Based on these findings, the partial structure (a) (Fig. 2) was proposed for this compound.

The ^{1}H-NMR spectrum of **15** exhibited the flavan H-2 and H-3 signals at δ 4.14 (dt, J=9, 1.5 Hz) and 4.00 (dd-like, J=7, 8 Hz), respectively, which were assigned on the basis of ^{1}H–^{1}H COSY spectral analysis. This H-2 signal showed cross peaks with an olefinic proton (H_b) signal at δ 6.48 (t, J=1.5 Hz) and a methine (H_c) signal at δ 4.08 (t, J=1.5 Hz). In addition, a mutual correlation was also observed between the H_b and H_c signals.

Further structural confirmation was obtained by ^{1}H–^{13}C long-range COSY spectral analysis, which displayed many correlations as shown in Fig. 1. Among these, the observation of the correlations of the H_c signal with the above-mentioned benzyl methine signal (δ 48.6) and the oxygen-bearing quaternary carbon signal (δ 91.8) were of particular importance, since connection between the partial structure (b) and the oxidized flavan B-ring structure became possible through the correlations of this H_c signal. Moreover, the chemical shift (δ 91.8) of the quaternary carbon, as well as the presence of a carboxyl carbon (δ 171.5) located close to H_c, indicated the existence of a γ-lactone ring as shown in Fig. 2, consistent with the negative FAB-MS data [m/z 1189 $(M-H)^-$].

The two-dimensional nuclear Overhauser effect spectrum (NOESY) clearly showed a strong correlation between the H_a and H_c signals, along with those between polyalcohol H-1 and H-3. These facts, combined with the inspection of the Dreiding model, clearly indicated that **15** has the partial stereostructure (c) (Fig. 3). As for the stereochemistry of the flavan C-ring, 2*R*- and 3*S*-configurations were deduced from the absence of the NOE cross peaks between the flavan H-2 and H_c signals, as well as the fact that (+)-catechin and (+)-gallocatechin (**3**) occur together in this plant. Furthermore, the atropisomerism of the HHDP group located at the polyalcohol C-4 and C-6 positions was concluded to be in the *S*-series by comparison of the ^{1}H-NMR chemical shifts of the HHDP singlets with those of compounds **5**—**8**.

On the basis of these findings, the structure of psiguavin was concluded to be as represented by the formula **15**. Psiguavin (**15**) was considered to be derived biosynthetically from eugenigrandin A (**7**) by successive oxidation, benzylic acid-type rearrangement and decarboxylation, followed by oxidative coupling, as shown in Chart 1.

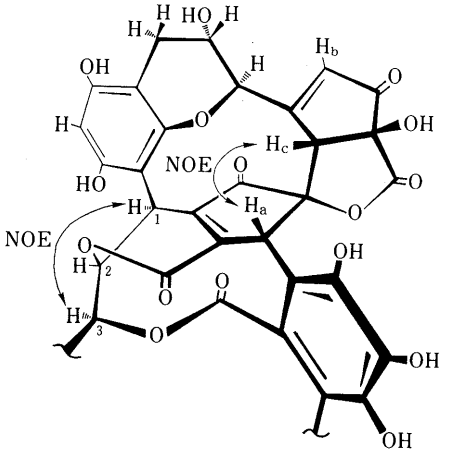


Fig. 3. Partial Stereostructure (c) of Psiguavin (**15**)

Experimental

Details of the instruments and chromatographic conditions used in this study are essentially the same as those described in the previous paper.[19]

Isolation of Tannins The dried bark (3.5 kg) of *Psidium guajava* L., collected in Belem, Para, Brazil, was extracted three times with 80% aqueous acetone at room temperature. After evaporation of acetone under reduced pressure, the resulting precipitates were removed by filtration. The filtrate was further concentrated and applied to a column of Sephadex LH-20. Elution with H_2O containing increasing amounts of MeOH gave two fractions. The first eluted fraction was chromatographed over MCI-gel CHP 20P with 20% aqueous MeOH to furnish valolaginic acid (400 mg), vescalagin carboxylic acid (72 mg) and grandinin (1.3 g). The second fraction was rechromatographed over Sephadex LH-20 eluted gradiently with H_2O and 10%, 20% and 30% aqueous MeOH to yield four fractions (II-1—II-4). Fraction II-1 was subjected to repeated chromatography over Sephadex LH-20 (EtOH), MCI-gel CHP 20P (H_2O–MeOH) and Bondapak C_{18}/Porasil B (H_2O–MeOH), giving (+)-catechin (*ca.* 1 g), (+)-gallocatechin (**3**) (*ca.* 2 g), procyanidin B-1 (16 mg), prodelphinidin B-1 (7 mg), 3,4,5-trimethoxyphenol 1-*O*-β-D-(2′,6′-di-*O*-galloyl)-glucopyranoside (16 mg) and 2,3-(*S*)-HHDP-6-*O*-galloyl-D-glucopyranose (10 mg). Chromatography of fraction II-2 over MCI-gel CHP 20P with H_2O–MeOH afforded pedunculagin (95 mg) and castalagin (5.8 g), while repeated chromatography of fraction II-3 over MCI-gel CHP 20P, Fuji-gel ODS G3 and Bondapak C_{18}/Porasil B gave casuarinin (136 mg), acutissimin A (**8**) (300 mg), eugenigrandin A (**7**) (2.8 g), mongolicain A (**10**) (141 mg), guajavin A (**5**) (86 mg), psidinins A (**9**) (560 mg), B (**11**) (86 mg) and C (**13**) (82 mg) and psiguavin (**15**) (134 mg). The final fraction, II-4, afforded acutissimin B (**2**) (13 mg) and guajavin B (**1**) (740 mg) on chromatography over MCI-gel CHP 20P with H_2O containing increasing proportions of MeOH.

Guajavin B (1) A pale brown amorphous powder, $[\alpha]_D^{21}$ +27.5° (c=1.1, MeOH). *Anal.* Calcd for $C_{56}H_{38}O_{32}\cdot 8H_2O$: C, 49.20; H, 3.98. Found: C, 49.14; H, 3.81. Negative FAB-MS m/z: 1221 $[M-H]^-$. ^{1}H-NMR (100 MHz, acetone-d_6+D_2O) δ: 2.5—2.8 [2H, gallocatechin (GC)-H-4], 4.17 (1H, d, J=12 Hz, H-6), 4.08 (1H, m, GC-H-3), 4.40 (1H, d, J=4 Hz, GC-H-2), 4.84 (1H, d, J=7 Hz, H-3), 4.87 (1H, d, J=12 Hz, H-6), 5.12 (1H, br s, H-2), 5.27 (1H, m, H-4), 5.65 (1H, d, J=7 Hz, H-5), 6.11 (1H, s, GC-H-8), 6.54 (2H, s, GC-H-2′, 6′), 6.64, 6.79 (each 1H, s, HHDP-H), 7.10 (1H, s, aromatic H). ^{13}C-NMR: Table I.

Methylation of 1 A mixture of **1** (100 mg), dimethyl sulfate (2 ml) and anhydrous potassium carbonate (2 g) in dry acetone (20 ml) was heated under reflux for 4 h. After cooling, the insoluble inorganic salts were removed by filtration, and the filtrate was chromatographed over silica gel with benzene containing increasing proportions of acetone to give the eicosamethyl ether as a white amorphous powder (50 mg), $[\alpha]_D^{20}$ −21.0° (c=0.33, $CHCl_3$). *Anal.* Calcd for $C_{76}H_{78}O_{32}\cdot 1/2H_2O$: C, 60.35; H,

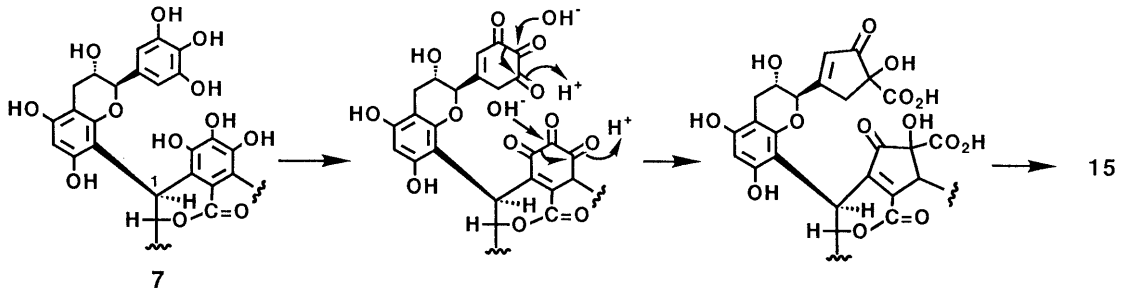


Chart 1. Possible Biosynthetic Pathway of Psiguavin (**15**) from Eugenigrandin A (**7**)

5.27. Found: C, 60.31; H, 5.43. FD-MS *m/z*: 1502 $[M]^+$. ^{1}H-NMR (100 MHz, $CDCl_3$) δ: 2.3—3.0 (2H, GC-H-4), 3.4—4.2 (OMe), 4.68 (1H, s, H-1), 4.70 (1H, d, J=10 Hz, GC-H-2), 4.87 (1H, d, J=8 Hz, H-3), 5.06 (1H, s, H-2), 5.39 (1H, t, J=8 Hz, H-4), 5.73 (1H, d, J=7 Hz, H-5), 6.29 (1H, s, GC-H-8), 6.72 (2H, s, GC-H-2′, 6′), 6.76, 6.88, 7.19 (each 1H, s, aromatic H). ^{13}C-NMR (20.05 MHz, $CDCl_3$) δ: 29.7 (GC-C-4), 37.9 (C-1), 65.4 (C-6), 68.4 (GC-C-3), 70.1 (C-4), 71.1 (C-3), 82.7 (GC-C-2), 96.8 (GCC-8), 104.4 (GC-C-4a), 106.1 (GC-C-2′, 6′), 155.2 (GC-C-8a), 156.7 (GC-C5), 159.1 (GC-C-7), 163.9, 164.9, 166.6, 167.8 (–COO–).

Preparation of 1 A mixture of vescalagin (**4**) (54 mg) and (+)-gallocatechin (**3**) (450 mg) in dry dioxane (5 ml) containing *p*-toluenesulfonic acid (2 mg) was heated at 0 °C for 1 h. The reaction mixture was concentrated to dryness under reduced pressure, and the residue was chromatographed over Sephadex LH-20 with H_2O containing increasing amounts of MeOH to give eugenigrandin A (**7**) (364 mg) and guajavin B (**1**) (183 mg).

Guajavin A (5) A pale brown amorphous powder, $[\alpha]_D^{19}$ +73.0° (c=1.0, MeOH). *Anal.* Calcd for $C_{56}H_{40}O_{32}\cdot 6H_2O$: C, 50.47; H, 3.93. Found: C, 50.55; H, 3.70. Negative FAB-MS *m/z*: 1223 $[M-H]^-$. The ^{1}H-NMR spectrum was complicated by rotational isomerism. ^{13}C-NMR: Table I. Circular dichroism (CD) ($c=1.0\times10^{-4}$, MeOH) $[\theta]^{20}$ (nm): 0 (298), 14400 (283), 0 (276), −30400 (268), 0 (254), 92400 (235), 0 (215), −57300 (208).

Methylation of 5 A mixture of **5** (25 mg), dimethyl sulfate (0.1 ml) and potassium carbonate (1 g) in dry acetone (10 ml) was refluxed with stirring for 4 h. The reaction mixture was worked up as described above to furnish the eicosamethyl ether as a white amorphous powder, $[\alpha]_D^{20}$ −8.1° (c=1.0, $CHCl_3$). *Anal.* Calcd for $C_{76}H_{80}O_{32}\cdot 1/2H_2O$: C, 60.27; H, 5.39. Found: C, 60.20; H, 5.41. FD-MS *m/z*: 1504 $[M-H]^-$. ^{13}C-NMR (25.05 MHz, $CDCl_3$) δ: 24.2 (GC-C-4), 37.1, 37.9 (1C in total, C-1), 55.3—61.4 (OMe), 63.7—82.0 (C-1—C-6, GC-C-2, 3), 89.0 (C-6), 103.2 (GC-C-2′, 6′), 106.4 (galloyl C-2, 6), 165.3, 167.9, 168.0, 168.6 (–COO–).

Preparation of 5 A mixture of stachyurin (20 mg) and (+)-gallocatechin (**3**) (26 mg) in dry dioxane containing *p*-toluenesulfonic acid (2 mg) was heated under reflux for 1.5 h. The reaction product was purified by chromatography over MCI-gel CHP 20P with H_2O–MeOH to give guajavin A (**5**) (11 mg).

Psidinin A (9) A pale brown amorphous powder, $[\alpha]_D^{26}$ −146.6° (c=1.0, MeOH). *Anal.* Calcd for $C_{55}H_{38}O_{31}\cdot 5H_2O$: C, 51.49; H, 3.61. Found: C, 51.45; H, 3.79. Negative FAB-MS *m/z*: 1191 $[M-H]^-$. ^{1}H-NMR (100 MHz, acetone-d_6+D_2O) δ: 2.52 (1H, dd, J=16, 5 Hz, GC-H-4), 2.84 (1H, dd, J=16, 5 Hz, GC-H-4), 4.09 (1H, d, J=12 Hz, H-6), 4.24 (1H, s, H-1), 4.37 (1H, s, –CH–), 4.53 (1H, d, J=12 Hz, H-6), 4.59 (1H, m, GC-H-3), 5.28 (1H, d, J=5 Hz, H-3), 5.37 (1H, br d, J=3 Hz, GC-H-2), 5.39—5.64 (2H, m, H-4 and H-5), 5.81 (1H, s, H-2), 6.14 (1H, s, GC-H-6), 6.24 (2H, s, GC-H-2′, 6′), 6.58, 6.64 (each 1H, s, HHDP-H), 7.08 (1H, s, aromatic H).^{13}C-NMR: Table I. CD (c=1.0×10^{-4}, MeOH) $[\theta]^{20}$ (nm): 0 (318), −19900 (237), 0 (215), 14200 (206).

Methylation of 9, Followed by Acetylation and Alkaline Methanolysis of 9 **9** (300 mg) was methylated in the same way as described above to give the heptadecamethyl ether as a white amorphous powder (195 mg), $[\alpha]_D^{20}$ −182.0° (c=0.8, $CHCl_3$). *Anal.* Calcd for $C_{72}H_{70}O_{31}\cdot 3H_2O$: C, 58.22; H, 5.16. Found: C, 58.27; H, 4.89. FD-MS *m/z*: 1430 $[M]^+$. ^{1}H-NMR (100 MHz, $CDCl_3$) δ: 2.4—2.8 (2H, GC-H-4), 3.6—4.0 (OMe), 4.39 (1H, s, –CH–), 6.12 (1H, s, GC-H-6), 6.23 (2H, s, GC-H-2′, 6′), 6.62, 6.63, 6.68 (each 1H, s, aromatic H). ^{13}C-NMR (25.05 MHz, $CDCl_3$) δ: 26.4 (GC-C-4), 45.2 (C-1), 56.0—62.0 (OMe), 64.8 (C-6), 67.7 (C-4), 71.0 (C-5), 72.4 (C-3), 79.8 (C-2), 82.1 (GC-C-2), 86.9 (GC-C-6), 161.9, 165.0, 165.9, 166.3, 167.8 (–COO–). The heptadecamethyl ether (20 mg) was acetylated overnight with a mixture of acetic anhydride and dry pyridine (1 ml, 1:1) at room temperature. Work-up as usual yielded the monoacetate as a white amorphous powder (13 mg), $[\alpha]_D^{20}$ −162.6° (c=0.5, $CHCl_3$). *Anal.* Calcd for $C_{74}H_{72}O_{32}\cdot 5/2H_2O$: C, 58.53; H, 5.11. Found: C, 58.67; H, 4.97. FD-MS *m/z*: 1472 $[M]^+$. ^{1}H-NMR (100 MHz, $CDCl_3$) δ: 1.61 (3H, s, CH_3COO–), 2.4—3.1 (2H, GC-H-4), 3.5—4.1 (OMe), 4.47 (1H, s, –CH–), 4.98 (1H, d, J=6 Hz, H-3), 5.1—5.5 (3H in total, m, H-2, 4, 5), 6.22 (1H, s, GC-H-6), 6.23 (2H, s, GC-H-2′, 6′), 6.52, 6.62, 6.68 (each 1H, s, aromatic H). Alkaline methanolysis of the monoacetyl heptadecamethyl ether (20 mg) in 2% NaOMe–MeOH yielded, among others, dimethyl (*S*)-hexamethoxydiphenoate (11 mg) as a colorless syrup, $[\alpha]_D^{20}$ −27.0° (c=1.1, $CHCl_3$).

Psidinin B (11) A pale brown amorphous powder, $[\alpha]_D^{21}$ −27.2° (c=1.0, MeOH). *Anal.* Calcd for $C_{55}H_{36}O_{31}\cdot 6H_2O$: C, 50.78; H, 3.72. Found: C, 50.56; H, 3.60. Negative FAB-MS *m/z*: 1191 $[M-H]^-$. ^{1}H-NMR (100 MHz, acetone-d_6+D_2O) δ: 2.63 (1H, dd, J=16, 5Hz, GC-H-4), 2.86 (1H, dd, J=16, 5 Hz, GC-H-4), 4.07 (1H, d, J=12 Hz, H-6), 4.08 (1H, s, H-1), 4.14 (1H, m, GC-H-3), 4.39 (1H, s, –CH–), 4.64 (1H, d, J=8 Hz, GC-H-2), 4.72 (1H, d, J=12 Hz, H-6), 5.20 (1H, d, J=6 Hz, H-3), 5.3—5.6 (2H in total, m, H-4, 5), 5.88 (1H, s, H-2), 6.21 (1H, s, GC-H-8), 6.51 (2H, s, GC-H-2′, 6′), 6.64, 6.68 (each 1H, s, HHDP-H), 6.95 (1H, s, aromatic H). ^{13}C-NMR: Table I. CD ($c=1.0\times10^{-4}$, MeOH) $[\theta]^{20}$ (nm): 0 (315), −9400 (299), 0 (284), 6800 (278), 0 (274), −57800 (237), 0 (225), 58100 (218), 0 (211), −69400 (205).

Psidinin C (13) A pale brown amorphous powder, $[\alpha]_D^{31}$ −47.4° (c=1.0, MeOH). *Anal.* Calcd for $C_{55}H_{38}O_{31}\cdot 6H_2O$: C, 50.70; H, 3.87. Found: C, 50.50; H, 3.87. Negative FAB-MS *m/z*: 1193 $[M-H]^-$. ^{1}H-NMR (270 MHz, acetone-d_6+D_2O) δ: 2.61 (1H, dd, J=16, 6 Hz, GC-H-4), 2.70 (1H, dd, J=16, 7 Hz, GC-H-4), 4.09 (1H, s, H-1), 4.16 (1H, d, J=12 Hz, H-6), 4.36 (1H, s, –CH–), 4.37 (1H, m, GC-H-3), 4.59 (1H, dd, J=12, 3 Hz, H-6), 5.19 (2H, d, J=6 Hz, H-3, GC-H-2), 5.37 (1H, br s, H-2), 5.63 (1H, d-like, J=7 Hz, H-5), 5.79 (1H, dd, J=6, 8 Hz, H-4), 6.09 (1H, s, GC-H-6), 6.42 (2H, s, GC-H-2′, 6′), 6.51, 6.63 (each 1H, s, HHDP-H), 7.00 (1H, s, aromatic H), 7.06 (2H, s, galloyl H). ^{13}C-NMR: Table I. CD ($c=1.0\times10^{-4}$, MeOH) $[\theta]^{20}$ (nm): −10600 (300), 13600 (280), 0 (273), −43600 (260), 0 (247), 23000 (232), 0 (224), −13100 (220).

Methylation of 13 **13** (40 mg) was methylated in the same manner as above to afford the heptadecamethyl ether as a white amorphous powder (18 mg), $[\alpha]_D^{20}$ −62.0 (c=0.5, $CHCl_3$). *Anal.* Calcd for $C_{72}H_{72}O_{31}\cdot 3H_2O$: C, 60.33; H, 5.06. Found: C, 60.37; H, 5.38. FD-MS *m/z*: 1448 $[M]^+$.

Psiguavin (15) A pale brown amorphous powder, $[\alpha]_D^{27}$ −62.9° (c=0.5, MeOH). *Anal.* Calcd for $C_{55}H_{34}O_{31}\cdot 19/2H_2O$: C, 48.50; H, 3.92. Found: C, 48.42; H, 3.99. Negative FAB-MS *m/z*: 1189 $[M-H]^-$. ^{1}H-NMR (270 MHz, acetone-d_6+D_2O) δ: 2.57 (1H, dd, J=8, 17 Hz, flavan (FA)-H-4), 3.00 (1H, dd, J=7, 17 Hz, FA-H-4), 3.98 (1H, dd, J=5.5, 12 Hz, H-6), 4.00 (1H, dd-like J=7, 8 Hz, FA-H-3), 4.08 (1H, t, J=1.5 Hz, H_c), 4.14 (1H, dt, J=9, 1.5 Hz, FA-H-2), 4.15 (1H, s, H-1), 4.97 (1H, dd, J=6, 12 Hz, H-6), 5.40 (1H, s, Ha), 5.55 (1H, dt-like, J=5.5, 6 Hz, H-5), 5.65 (1H, t-like, J=5.5 Hz, H-4), 5.69 (1H, d, J=5.5 Hz, H-3), 5.90 (1H, s, H-2), 6.28 (1H, s, FA-H-6), 6.48 (1H, t, J=1.5 Hz, Hb), 6.72, 6.73 (each 1H, s, HHDP-H), 7.00 (1H, aromatic H). ^{13}C-NMR: Table I.

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