Four New C-Glycosidic Ellagitannins, Castacrenins D—G, from Japanese Chestnut Wood (*Castanea crenata* SIEB. *et* ZUCC.)

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Received May 19, 1997; accepted July 11, 1997

In the course of studies on polyphenol metabolism in wood, four new C-glycosidic ellagitannins named castacrenins D—G were isolated from the wood of the Japanese chestnut tree (*Castanea crenata*). Castacrenins D and F are related to vescalagin and have a gallic acid and an ellagic acid moiety, respectively. Castacrenins E and G are oxidative metabolites of castacrenins D and F, respectively, in which a pyrogallol ring of each C-glycosidic ellagitannin unit is replaced by a cyclopentenone ring.

Key words tannin; *Castanea crenata*; ellagitannin; polyphenol; chestnut

The wood of the Japanese chestnut tree (*Castanea crenata* SIEB. *et* ZUCC., Fagaceae) is very durable, and this is attributed to its extensive heartwood with a high concentration of tannins (about 8%). It is known that tannins in heartwood are mainly biosynthesized in parenchymal cells at the sapwood-heartwood transitional region. As the tree grows, the parenchymal cells of the inner sapwood die and the heartwood extends. Hence, tannins in the inner heartwood have been stored for a long period since having been biosynthesized. We are interested in the metabolism of tannins in the wood of Japanese chestnut tree and previously pointed out some characteristic features.[2)] 1) Hamamelitannin and proanthocyanidins, which are major components of the bark, were completely absent in the wood. 2) Although almost no polyphenolic substances exist near the cambium, two dominant C-glycosidic ellagitannins, castalagin (**1**) and vescalagin (**2**),[3,4)] were largely accumulated in the sapwood-heartwood transitional region, and their concentration was lower in inner heartwood. 3) In the heartwood, instead, monomeric (castacrenins A—C) and oligomeric metabolites (roburins A and D,[5)] and castaneanins A—D) were generated by intramolecular and intermolecular dehydration, respectively, of **1** and **2**. Further chemical study on polyphenols in the chestnut wood led us to the isolation of four additional minor C-glycosidic ellagitannins named castacrenins D—G, which were also metabolites of **1** and **2**. This paper deals with the isolation and structural elucidation of these tannins.

Extraction from the outer heartwood with aqueous acetone and fractionation by Sephadex LH-20 column chromatography as described in the previous paper afforded seven fractions.[2)] Among them, the fourth and sixth fractions were further separated by a combination of column chromatographies over MCI-gel CHP20P, Sephadex LH-20, Cosmosil 75C_{18}-OPN, TSK-gel Toyopearl HW40F and Chromatorex ODS with various elution systems to yield castacrenins D (**3**), E (**4**), F (**5**) and G (**6**).

Castacrenin D (**3**) was obtained as a white amorphous powder and gave a dark blue coloration with the $FeCl_3$ reagent. The ^{1}H-NMR spectrum of **3** (Table 1) was related to that of vescalagin (**2**) and acutissimin A (**7**), a complex tannin in the bark of *Quercus* species[4,6,7)] and showed seven aliphatic signals arising from an acylated open-chain glucose, besides four aromatic singlets. In the ^{13}C-NMR spectrum (Table 2), the chemical shifts of the signals due to the glucose moiety were similar to those of **7** and different from those of **2** in respect of the chemical shift of C-1. This fact implied that an additional aromatic ring was attached to the C-1 of the vescalagin unit through a C–C bond. The molecular weight estimated by negative ion FAB-MS (*m/z*: 1085, $[M-H]^-$) was 152 mass units larger than that of **2**, a difference which coincids with the mass of a galloyl group. From this result, the additional aromatic ring was deduced to be a gallic acid and this was confirmed by the following chemical evidence: methylation of **3** with $(CH_3)_2SO_4$ and K_2CO_3 yielded a nonamethylate (**3a**) [*m/z*: 1353 $(M+H)^+$], which was further methanolyzed to yield dimethyl (*S*)-hexamethoxydiphenate (**3b**) and a methanolysate (**3c**). The appearance of a $(M+H)^+$ peak at *m/z* 999 in the positive ion FAB-MS of **3c** and the low-field shifts of H-2 (δ 5.09, dd, $J=1.1$, 2.7 Hz) and H-3 (δ 4.60, dd, $J=1.6$, 2.7 Hz) in the ^{1}H-NMR spectrum indicated that **3c** was an analogue of the methanolysate obtained from **7** by similar derivatization.[6)] The configuration of the C-1 position was deduced to be the same as that of **2** and **7** from the similar small coupling constant between H-1 and H-2 ($J_{1,2} \leqq 1$ Hz).[4)] Based on the above spectroscopic and chemical evidence, the structure of castacrenin D was concluded to be represented by the formula **3**.

Castacrenin E (**4**) was isolated as a tan amorphous powder and exhibited an $[M-H]^-$ peak at *m/z* 1055 in the negative ion FAB-MS, which was 30 mass units less than that of **3**. The ^{1}H- and ^{13}C-NMR spectra (Tables 1 and 2) showed signals due to an open-chain glucose along with a number of aromatic and ester carbons, indicating that this compound is also a C-glycosidic ellagitannin. In addition to these signals, the appearance of an aliphatic proton singlet [δ 4.47 (Cp-1)] in the ^{1}H-NMR spectrum, and a carbonyl [δ 195.5 (Cp-4)], two olefinic [δ 137.1 (Cp-2) and 149.4 (Cp-3)] and two aliphatic [δ 48.6 (Cp-1) and 91.2 (Cp-5)] carbon signals in the ^{13}C-NMR spectrum was similar to those due to the cyclopentenone ring of

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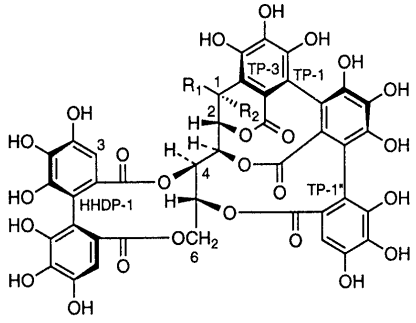
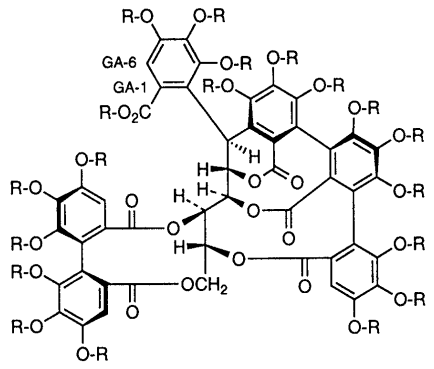
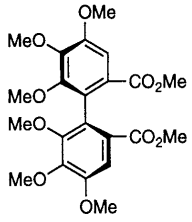


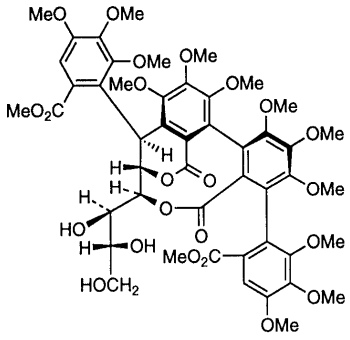
1 : R_1 = H, R_2 = OH
2 : R_1 = OH, R_2 = H



3 : R = H
3a : R = Me



3b



3c

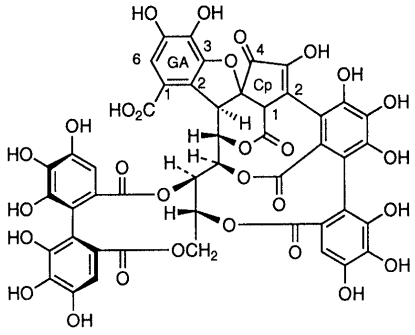


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Table 1. ^{1}H-NMR Spectral Data for **1**—**6**, Acutissimin A (**7**) and Mongolicain A (**8**) (in Acetone-d_6)

	1[a]	**2**[a]	**3**[b]	**4**[c]	**5**[c]	**6**[d]	**7**[7a]	**8**[a]
H-1	5.72 (d, 5)	4.92 (d, 2)	5.34 (s)	4.14 (s)	6.03 (s)	4.54 (s)	4.84 (s)	4.23 (s)
H-2	5.06 (dd, 1, 5)	5.30 (dd, 2, 2)	5.24 (br s)	5.44 (d, 1)	5.39 (s)	5.59 (s)	5.20 (s)	5.80 (s)
H-3	5.04 (dd, 1, 7)	4.59 (dd, 2, 7)	5.01 (br d, 8)	5.32 (d, 8)	5.15 (d, 8)	5.45 (d, 8)	4.76 (d, 8)	5.25 (d, 8)
H-4	5.25 (dd, 7, 8)	5.23 (dd, 7, 8)	5.30 (t, 8)	5.62 (t, 8)	5.39 (t, 8)	5.71 (t, 8)	5.28 (t, 8)	5.61 (t, 8)
H-5	5.61 (dd, 2, 8)	5.66 (dd, 3, 13)	5.64 (br d, 8)	5.53 (d, 8)	5.66 (d, 8)	5.54 (d, 8)	5.60 (d, 8)	5.54 (dd, 2, 8)
H-6a	5.09 (dd, 2, 13)	5.08 (dd, 3, 13)	4.72 (dd, 2, 13)	4.77 (dd, 2, 13)	4.72 (dd, 2, 12)	4.74 (dd, 2, 13)	4.60 (d, 12)	4.55 (dd, 2, 12)
H-6b	4.02 (d, 13)	4.08 (d, 13)	4.05 (d, 13)	3.97 (d, 13)	4.00 (d, 12)	3.96 (d, 13)	4.12 (d, 12)	4.05 (d, 12)
Cp-1				4.47 (s)		4.63 (s)		4.38 (s)
Arom. H	6.67 6.81 6.82	6.67 6.82 6.82	6.61 6.71 6.77 7.31	6.47 6.60 6.65 7.30	6.56 6.57 6.77 7.62	6.47 6.61 6.68 7.63	6.56 6.76 7.08	6.59 6.65 7.08

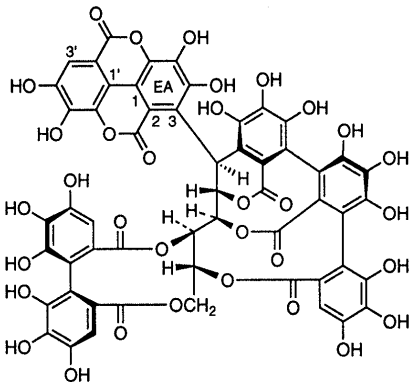
a) Measured at 400 MHz. *b*) Measured at 270 MHz. *c*) Measured at 500 MHz. *d*) Measured at 300 MHz.

mongolicain A (**8**), which is a complex tannin isolated from *Quercus* species.[4,7,8] The presence of the cyclopentenone structure in **4** was confirmed by observation of the heteronuclear multiple bond connectivity (HMBC) correlation as shown in Fig. 1: the aliphatic proton (δ 4.47) was correlated with the two olefinic carbons and a carboxyl carbon (δ 167.2), which was correlated with the H-2 of the open-chain glucose. Three-bond long-range couplings were also observed between the carbonyl carbon at δ 195.5 (Cp-4) and the H-1 of the glucose and between the oxygen-bearing aliphatic carbon at δ 91.2 (Cp-5) and the H-2 of glucose. The correlation pattern was analogous to those observed in the spectrum of **8**. Because the difference (30 mass units) of molecular weight between **4** (1056) and **3** (1086) was the same as that between **8** (1178) and **7** (1208), the remaining group attached to the C-1 of the

Table 2. ^{13}C-NMR Spectral Data for **1**—**6**, Acutissimin A (**7**) and Mongolicain A (**8**) (in Acetone-d_6+D_2O)

	1[a]	**2**[a]	**3**[b]	**4**[c]	**5**[c]	**6**[d]	**7**[a]	**8**[a]
C-1	67.4	66.1	41.0	48.5	40.7	47.7	38.2	48.0
C-2	74.5	78.3	78.5	81.7	77.7	79.7	78.0	78.2
C-3	66.7	69.1	72.5	73.4	72.6	72.4	72.7	72.9
C-4	69.7	70.0	69.9	67.6	69.7	66.8	71.5	68.9
C-5	71.7	71.7	71.2	71.3	71.0	70.4	71.9	71.6
C-6	65.8	66.0	66.0	64.9	65.9	63.8	66.0	65.4
Cp-1				48.6		47.3		50.7
Cp-2				137.1		137.7		140.4
Cp-3				149.4		149.4		149.4
Cp-4				195.5		194.4		197.2
Cp-5				91.2		90.7		89.8
COO	165.3	165.1	165.8	163.5	159.6	158.68	166.1	163.9
	166.0	165.8	167.0	165.9	160.6	158.73	167.7	167.1
	67.1	166.9	167.3	166.8	165.6	162.5	168.1	167.4
	167.7	167.4	167.7	167.2	166.0	165.2	168.3	168.2
	169.7	169.5	169.4	167.4	166.2	166.0	169.6	169.7
			170.0	168.7	166.7	166.1		
					169.1	168.1		

a) Measured at 100 MHz. *b*) Measured at 25 MHz. *c*) Measured at 125 MHz. *d*) Measured at 75 MHz.



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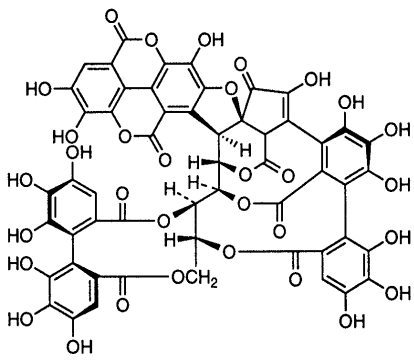

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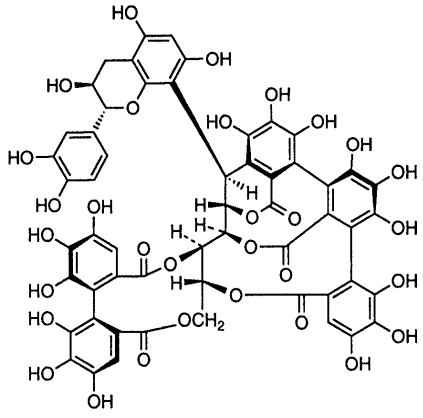

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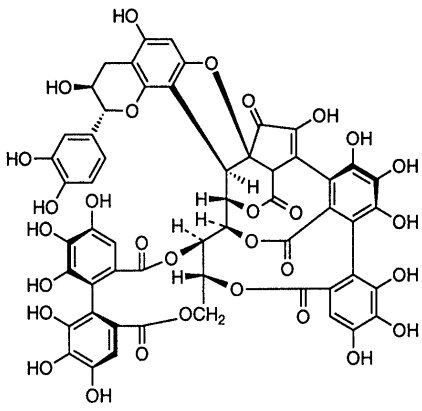

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glucose of **4** was deduced to be a gallic acid moiety. The HMBC correlation shown in Fig. 1 was consistent with this assignment. Formation of an ether linkage between a phenolic oxygen of the gallic acid moiety and one of the aliphatic carbons (Cp-5) of the cyclopentenone ring was also deduced from the molecular weight and the ^{13}C-NMR chemical shift of Cp-5 (δ 91.2), which was similar to that of **8** (δ 89.8). The small coupling constants of glucose H-1, H-2 and H-3 ($J_{1,2}<1$ Hz, $J_{2,3}=1$ Hz), which were also similar to those of **8**, confirmed the same configuration at the glucose C-1 of these compounds.[4] Furthermore, construction of a Dreiding model of **4** indicated that the benzyl methine proton (Cp-1) of the cyclopentenone ring must have β-configuration, because its fused ring system, including two aromatic rings, two cyclopentenes and 6- and 10-membered lactone rings, was so rigid that an alternative model could not be constructed. On the basis of these observations, the structure of castacrenin E was deter-

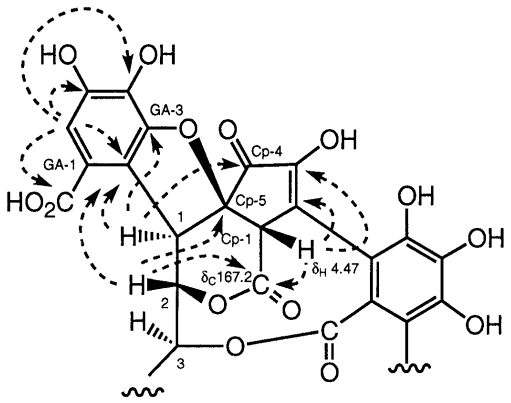

Fig. 1. Selected HMBC Correlations for Castacrenin E (**4**)

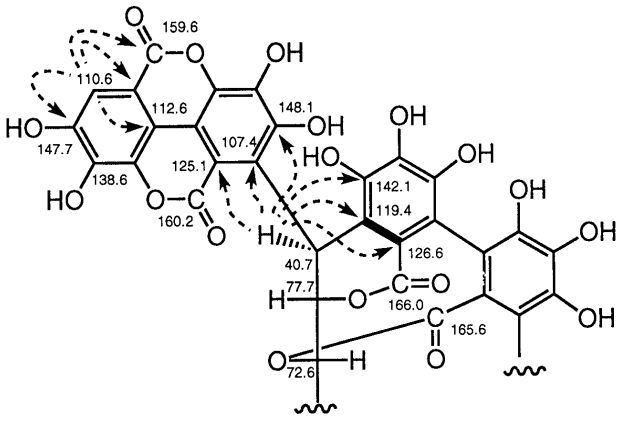

Fig. 2. Selected HMBC Correlations for Castacrenin F (**5**)

mined to be as represented by the formula **4**.

Castacrenin F (**5**) was obtained as a yellow amorphous powder and showed a greenish blue coloration with $FeCl_3$ reagent. The ^{1}H-NMR spectrum (Table 1) was closely related to that of **3**, showing seven aliphatic signals arising from an open-chain glucose of the vescalagin unit, together with four aromatic singlets, among which the H-1 of the glucose (δ 6.03) and one (δ 7.62) of the aromatic protons were observed at significantly lower field compared to those of **3**. The ^{13}C-NMR spectrum (Table 2) was also related to that of **3** and indicated that **5** is a C-glycosidic ellagitannin having an additional aromatic ring at C-1 of the vescalagin unit. The most notable difference of the spectra was the appearance of two carboxyl carbon signals at δ 159.6 and 160.6 in the spectrum of **5**, the chemical shifts of which were similar to those of ellagic acid and ellagitannin metabolites having α, β; γ, δ-unsaturated bis-δ-lactone structures.[9] Furthermore, the molecular weight of **5** (1218) estimated from the negative ion FAB-MS [m/z: 1217 $(M-H)^-$] coincided with the sum of the mass of ellagic acid (302) and the vescalagin unit (917). These observations indicated that an ellagic acid moiety was attached to C-1 of the vescalagin unit in the molecule of **5**, and this was strongly supported by the HMBC correlations as shown in Fig. 2. Thus, the structure of castacrenin F was concluded to be as shown in **5**.

Castacrenin G (**6**) exhibited an $(M-H)^-$ peak at m/z 1187 in the negative ion FAB-MS, which is 30 mass units less than that of **5**. This difference of the molecular mass was the same as that between **4** and **3** suggesting a similar structural relationship. The ^{1}H-NMR spectrum (Table 1) resembled that of **4**, except for the large low field shift of H-1 ($\Delta\delta$ 0.30) and one (δ 7.63, $\Delta\delta$ 0.33) of the aromatic protons. As described above, these low field shifts were similarly observed in the spectrum of **5** when it was compared with that of **3**, implying the presence of an ellagic acid moiety at the C-1 position of the open-chain glucose. This was further supported by the observation of two carboxyl signals at δ 158.68 and 158.73 due to an α, β; γ, δ-unsaturated bis-δ-lactone in the ^{13}C-NMR spectrum (Table 2). Furthermore, the appearance of carbon and proton resonances due to a cyclopentenone ring (Tables 1 and 2) indicated a partial structure similar to that of **4**. From these spectroscopic observations, the structure of castacrenin G was deduced to be as represented by the formula **6**.

Castacrenins D—G were probably generated by condensation between **2** (or **1**) and gallic acid (for **3** and **4**) or ellagic acid (for **5** and **6**), followed by oxidative decarboxylation at the aromatic ring attached to C-1 of the vescalagin unit for **4** and **6**. Castacrenin F (**5**) may also be a partial hydrolysate derived from a terminal unit of roburins[5] and castaneanins,[2] in which the C-1 carbon of the vescalagin unit is attached to the hexahydroxydiphenoyl (HHDP) group of another vescalagin (or castalagin) unit. Atropisomerism of the HHDP and triphenyl groups of **3**—**6** was also deduced to be the same as in **1** and **2**[10] from this biogenetic relationship.

Experimental

The instruments and chromatographic conditions used throughout this work were the same as described in the preceding paper.[2]

Isolation The outer heartwood (6 kg) was extracted with acetone–H_2O (7:3, v/v) and fractionation by Sephadex LH-20 column chromatography as described in the previous paper[2] afforded seven fractions. Among these fractions, fr. 4 (155 g) was passed through MCI gel CHP 20P (60% MeOH) to remove non-polar substances, and then separated by Sephadex LH-20 chromatography (20→80% MeOH, stepwise gradient elution) to give vescalagin (**2**, 33 g), castalagin (**1**, 1.1 g) and crude castacrenin D, which was further purified by Cosmosil 5C_{18}-OPN chromatography (0→40% MeOH) (**3**, 1.38 g). Fr. 6 (40 g) was also passed through MCI-gel CHP 20P (60% MeOH) and subjected successively to chromatographies on TSK-gel Toyopearl HW40F (20→100% MeOH, stepwise gradient elution), Chromatorex ODS (0→40% MeOH) and MCI gel CHP20P (0→60% MeOH) to give castacrenins E (**4**, 159 mg), F (**5**, 182 mg) and G (**6**, 81 mg).

Castacrenin D (3) A white amorphous powder, $[\alpha]_D^{28}$ −29.6° (c=0.6, MeOH). *Anal.* Calcd for $C_{48}H_{30}O_{30}\cdot H_2O$: C, 52.19; H, 2.92. Found: C, 52.03; H, 3.23. Negative ion FAB-MS m/z: 1085 $(M-H)^-$. ^{1}H-NMR (300 MHz, acetone-d_6): Table 1. ^{13}C-NMR (25 MHz, acetone-d_6 + D_2O, signals of aliphatic and carboxyl carbons are listed in Table 2) δ: 107.1, 108.5, 110.0, 111.6 (CH), 113.8, 114.1, 114.4, 114.9, 116.0, 116.5, 117.0, 121.1, 121.7, 121.9, 124.9, 125.3, 125.9, 127.2, 127.9, 135.5(2C), 135.6, 136.4(2C), 137.6, 143.2, 143.4, 144.1, 144.3, 144.5, 144.7, 144.9, 145.1, 145.4, 145.6, 147.1.

Methylation of 3 A mixture of **3** (0.5 g), $(CH_3)_2SO_4$ (4 ml) and anhydrous K_2CO_3 (4 g) in dry acetone (30 ml) was heated under reflux for 3 h. After removal of the inorganic precipitates by filtration, the filtrate was concentrated under reduced pressure and the syrup was subjected to chromatography on silica gel (40 g) with benzene–acetone (9:1) to give a nonadecamethylate (**3a**) as colorless needles (361 mg) from MeOH, mp 259—260 °C, FAB-MS m/z: 1353 $(M+H)^+$. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 3.43, 3.46, 3.49(×2), 3.57, 3.66, 3.71, 3.78, 3.79, 3.86, 3.89, 3.90, 3.91, 3.93(×2), 3.94, 3.95, 4.07, 4.17 (each 3H, s, OMe), 4.08 (1H, d, J=12 Hz, H-6), 4.72 (1H, dd, J=2, 12 Hz, H-6), 4.88 (1H, s, H-2), 5.11 (1H, d, J=8 Hz, H-3), 5.38 (1H, s, H-1), 5.45 (1H, t, J=8 Hz, H-4), 5.80 (1H, d, J=8 Hz, H-5), 6.74, 6.78, 6.91, 7.18 (each 1H, s).

Methanolysis of 3a Compound **3a** (204 mg) was treated with 0.5% NaOMe in MeOH (10 ml) at room temperature for 2 d. The mixture was neutralized with Amberlite IR-120B (H^+ form) resin, and the solvent was evaporated off under reduced pressure. The residue was chromatographed on silica gel. Elution with benzene–acetone (19 : 1—4 : 1) afforded dimethyl (*S*)-hexamethoxydiphenate (**3b**, 40 mg) as a colorless syrup, $[\alpha]_D^{28}$ −26.6° (c=0.6, $CHCl_3$), recovered **3a** (50.3 mg), and a methanolysate **3c** (73 mg) as a white powder. FAB-MS m/z: 999 $(M+H)^+$, 967 $(M-MeOH)^+$. *Anal.* Calcd for $C_{48}H_{54}O_{23}$: C, 57.71; H, 5.45. Found: C, 57.50; H, 5.58. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.30, 3.52, 3.55, 3.58, 3.73, 3.81, 3.89, 3.90, 3.91, 3.935, 3.940(×2), 4.09, 4.15 (each 3H, s, OMe), 3.50 (1H, d, J=12 Hz, H-6), 3.66 (2H, m, H-4 and H-6), 3.89 (1H, H-5, overlapped with Me signal), 4.60 (1H, dd, J=1.6, 2.7 Hz, H-3), 4.87 (1H, d, J=1.1 Hz, H-1), 5.09 (1H, dd, J=1.1, 2.7 Hz, H-2), 7.20, 7.34 (each 1H, s).

Castacrenin E (4) A tan amorphous powder, $[\alpha]_D^{28}$ −165.3° (c=0.7, MeOH). *Anal.* Calcd for $C_{47}H_{28}O_{29}\cdot 8H_2O$: C, 47.01; H, 3.69. Found: C, 47.35; H, 3.67. Negative ion FAB-MS m/z: 1055 $(M-H)^-$. ^{1}H-NMR (500 MHz, acetone-d_6): Table 1. ^{13}C-NMR (125 MHz, acetone-d_6 + D_2O, signals of glucose, cyclopentenone and carboxyl carbons are listed in Table 2) δ: 107.4 (CH), 108.0 (CH), 108.9 (CH) , 111.9, 112.7 [gallic acid (GA)-6], 113.4, 115.1, 115.8, 116.3, 117.7, 123.8 (GA-2), 124.9, 125.1, 127.2, 127.5, 134.9 (GA-4), 135.8, 135.9, 136.7, 136.8, 143.7, 144.4, 144.5, 144.6, 144.9, 145.1, 145.3, 145.6, 147.4 (GA-5), 149.0 (GA-3).

Castacrenin F (5) A yellow amorphous powder, $[\alpha]_D^{28}$ −105.3° (c=0.9, MeOH). *Anal.* Calcd for $C_{55}H_{30}O_{33}\cdot 7H_2O$: C, 49.12; H, 3.30. Found: C, 49.13; H, 3.40. Negative ion FAB-MS m/z: 1217 $(M-H)^-$. ^{1}H-NMR (500 MHz, acetone-d_6): Table 1. ^{13}C-NMR (125 MHz, acetone-d_6 + D_2O, signals of glucose and carboxyl carbons are listed in Table 2) δ: 106.9 (HHDP-3), 108.3 [ellagic acid (EA)-3], 108.5 [triphenyl group (TP)-3′], 109.4, 109.8 (HHDP-3′), 111.5 (EA-3′), 113.6 (EA-1′), 113.7, 114.0 (TP-1″), 114.5, 114.6, 114.8 (HHDP-1′), 116.2 (HHDP-1), 116.6, 120.2 (TP-3), 124.9, 125.7, 126.0 (EA-2), 127.5 (TP-2), 128.2, 135.2, 135.5 (HHDP-5′), 136.2 (TP-5″), 136.5, 136.7 (HHDP-5), 137.5, 138.8, 139.6 (EA-5′), 143.1 (TP-4), 144.1, 144.5, 144.7, (HHDP-4), 145.3 (HHDP-4′), 145.5 (TP-4″), 148.6 (EA-4′), 148.9 (EA-4), 159.6 (EA-7′), 160.6 (EA-7), 165.6 (TP-7′), 166.0 (TP-7), 166.2 (HHDP-7), 166.7 (TP-7″), 169.1 (HHDP-7′).

Castacrenin G (6) A tan amorphous powder, $[\alpha]_D^{28}$ −36.3° (c=0.4, MeOH). *Anal.* Calcd for $C_{54}H_{28}O_{32}\cdot 9/2H_2O$: C, 51.08; H, 2.94. Found: C, 51.28; H, 3.43. Negative ion FAB-MS m/z: 1187 $(M-H)^-$. ^{1}H-NMR (300 MHz, acetone-d_6): Table 1. ^{13}C-NMR (75 MHz, acetone-d_6 + D_2O, signals of glucose, cyclopentenone and carboxyl carbons are listed in Table 2) δ: 104.7, 106.1, 106.4, 107.0, 108.0, 108.3, 109.0, 110.5, 111.1, 112.3, 112.4, 114.1, 115.3, 115.3, 123.76, 123.83, 125.7, 126.1, 126.2, 134.9, 135.68, 135.71, 136.0, 136.5, 137.8, 139.1, 142.9, 143.5, 143.6, 143.9, 144.0, 144.4, 144.7, 148.1, 148.2.

Acknowledgment We thank Mr. K. Inada and Mr. N. Yamaguchi of Nagasaki University for NMR and MS measurements. This work was supported by a Grant-in-Aid for Scientific Research (No. 05671753) from the Ministry of Education, Science and Culture of Japan.

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