Tannins of Rosaceous Plants. IX.[1] Rugosins D, E, F and G, Dimeric and Trimeric Hydrolyzable Tannins with Valoneoyl Group(s), from Flower Petals of *Rosa rugosa* THUNB.

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Three dimeric hydrolyzable tannins having a valoneoyl group, rugosins D (1), E (2) and F (3), and a trimeric hydrolyzable tannin having two valoneoyl groups, rugosin G (4), were isolated from flower petals of *Rosa rugosa* (Rosaceae), and their structures including the orientation of the valoneoyl groups were established.

Keywords tannin; dimeric hydrolyzable tannin; trimeric hydrolyzable tannin; *Rosa rugosa*; Rosaceae; valoneoyl group; rugosin D; rugosin E; rugosin F; rugosin G

Rosaceous plants contain a large variety of oligomeric hydrolyzable tannins.[2] One of these plants, *Rosa rugosa* THUNB., has been found to contain dimeric and trimeric hydrolyzable tannins having valoneoyl group(s) as a structural unit. This paper deals with the isolation and structure determination of these tannins.[3]

Results and Discussion

The ethyl acetate extract obtained from the aqueous acetone homogenate of flower petals of *Rosa rugosa* was subjected to column chromatography on Sephadex LH-20. Four new tannins were eluted from the column after monomeric hydrolyzable tannins,[1] and were named rugosins D (**1**), E (**2**), F (**3**) and G (**4**).

Rugosin D (**1**), a light-brown powder, showed the $[M+H]^+$ ion peak at *m/z* 1875, and the $[M+Na]^+$ ion peak at *m/z* 1897, in the fast-atom bombardment mass spectrum (FAB-MS). These ion peaks indicate its molecular formula to be $C_{82}H_{58}O_{52}$, which corresponds to a dimeric hydrolyzable tannin. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum (500 MHz, in acetone-d_6) of **1** showed that this tannin consists of five galloyl groups [δ 7.12 (2H, s), 7.01 (2H, s), 7.00 (4H, s) and 6.97 (2H, s)], a hexahydroxydiphenoyl (HHDP) group and a valoneoyl (Val) group [δ 7.12 (Val H_C), 6.65 (HHDP H_B), 6.48, 6.46 (Val H_A and HHDP H_A) and 6.24 (Val H_B) (1H each, s)], and two β-D-glucopyranose cores (see Table I). A positive Cotton effect ($[\theta]_{225}$ $+2.4\times10^5$) in the short-wavelength region[4] of the circular dichroism (CD) spectrum of **1** indicated that both the valoneoyl and HHDP groups have the (*S*)-configuration. Methylation of **1** afforded a nonacosa-*O*-methyl derivative (**5**).

The chemical shifts of glucose protons in the ^{1}H-NMR spectrum of **1** indicated that all the hydroxyl groups on the two glucopyranose cores are acylated. The large difference in the chemical shifts of the two protons on C-6 of each glucose core ($\Delta\delta$ 1.49 and 1.52) showed[5] that the two HHDP residues (including the HHDP moiety of the valoneoyl group) are on O-4—O-6 of the two glucose cores. The six galloyl residues (including the galloyl moiety of the valoneoyl group) are hence on O-1, O-2 and O-3 of the two glucose cores. Rugosin D is therefore composed of two molecules of tellimagrandin II (**6**).[5-7]

The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **1** (125.7 MHz, in actone-d_6) showed six pairs of glucose carbon signals [δ 93.5, 93.1 (C-1); 71.7 (2C) (C-2); 73.2, 73.1 (C-3); 70.6, 70.5 (C-4); 72.9, 72.8 (C-5); 63.0, 62.9 (C-6)]. They were almost the same as those of the corresponding carbons in **6** [δ 93.8 (C-1), 71.8 (C-2), 73.3 (C-3), 70.8 (C-4), 73.1 (C-5), 63.1 (C-6)],[8] and substantiated the location of each acyl group on the two glucose cores as described above. The only notable upfield shift (0.7 ppm)

TABLE I. ^{1}H-NMR Spectral Data (500 MHz) for Glucose Residues in Rugosins D (**1**), E (**2**) and F (**3**)

	Rugosin D (**1**)[a]	Rugosin E (**2**)[b]		Rugosin F (**3**)[b]
		α-Anomer	β-Anomer	
Glucose core R[c]				
H-1	6.17 (d, J=8 Hz)	5.51 (d, J=3.5 Hz)	5.04 (d, J=8 Hz)	6.16 (d, J=8.5 Hz)
H-2	5.60 (dd, J=8, 10 Hz)	5.09 (dd, J=3.5, 10 Hz)	5.25 (dd, J=8, 10 Hz)	5.14 (t, J=9 Hz)
H-3	5.82 (t, J=10 Hz)	5.83 (t, J=10 Hz)	5.57 (t, J=10 Hz)	5.41 (t, J=9.5 Hz)
H-4	5.15 (t, J=10 Hz)[d]	5.04 (t, J=10 Hz)	5.04 (t, J=10 Hz)	5.08 (t, J=10 Hz)
H-5	4.51 (dd, J=6.5, 10 Hz)	4.60 (ddd, J=1, 6.5, 10 Hz)	4.21 (dd, J=6.5, 10 Hz)	4.44 (dd, J=6.5, 10 Hz)[e]
H-6	5.30 (dd, J=6.5, 13 Hz)	5.18 (dd, J=6.5, 13 Hz)	5.19 (dd, J=6.5, 13 Hz)	5.26 (dd, J=6.5, 13.5 Hz)[f]
	3.78 (d, J=13 Hz)	3.66 (d, J=1, 13 Hz)	3.73 (d, J=13 Hz)	3.78 (d, J=13.5 Hz)
Glucose core L[c]				
H-1	6.12 (d, J=8 Hz)	6.08 (d, J=8 Hz)	6.08 (d, J=8 Hz)	6.08 (d, J=8 Hz)
H-2	5.52 (dd, J=8, 10 Hz)	5.55 (dd, J=8, 10 Hz)	5.54 (dd, J=8, 10 Hz)	5.23 (dd, J=8, 9.5 Hz)
H-3	5.77 (t, J=10 Hz)	5.78 (t, J=10 Hz)	5.78 (t, J=10 Hz)	5.77 (t, J=9.5 Hz)
H-4	5.16 (t, J=10 Hz)[d]	5.15 (t, J=10 Hz)	5.15 (t, J=10 Hz)	5.16 (t, J=10 Hz)
H-5	4.47 (dd, J=6.5, 10 Hz)	4.46 (dd, J=6.5, 10 Hz)	4.45 (dd, J=6.5, 10 Hz)	4.45 (dd, J=6.5, 10 Hz)[e]
H-6	5.30 (dd, J=6.5, 13 Hz)	5.27 (dd, J=6.5, 13 Hz)	5.27 (dd, J=6.5, 13 Hz)	5.27 (dd, J=6.5, 13 Hz)[f]
	3.81 (d, J=13 Hz)	3.80 (d, J=13 Hz)	3.79 (d, J=13 Hz)	3.80 (d, J=13 Hz)

a) In acetone-d_6, at 30 °C. *b*) In acetone-d_6+D_2O, at ambient temperature. *c*) See each structural formula. *d*—*f*) The assignments with the same superscript may be interchanged.

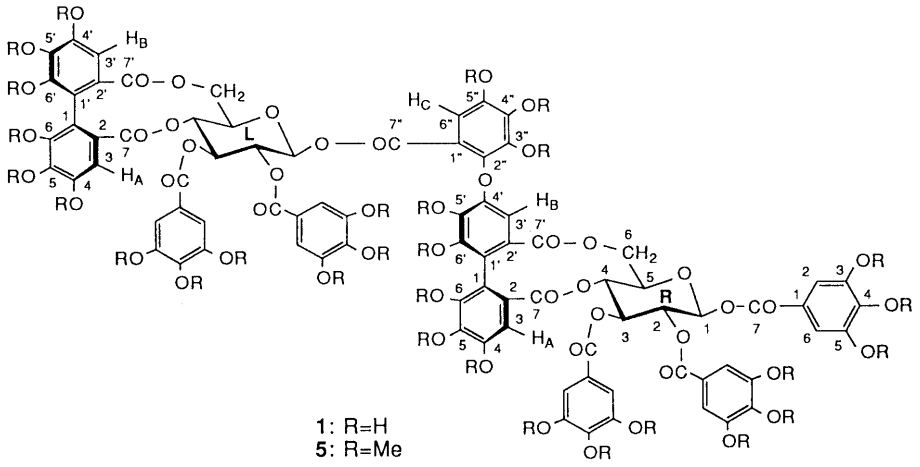
of one of the anomeric carbons at δ 93.1, relative to the anomeric carbon of **6**, is ascribable to an effect of steric compression due to the substitution of the valoneoyl group for the galloyl group on this anomeric center in **6**. Thus, the galloyl part of the valoneoyl group was assigned to be on O-1 of glucose core L in formula **1**.

A remarkable upfield shift of the H_B signal (δ 6.24) of the valoneoyl group in the ^{1}H-NMR spectrum of **1**, relative to one of the two HHDP protons (on the glucose O-6 side) of **6** (δ 6.67), indicated[1] that the galloyl moiety of the valoneoyl group is on the glucose O-6 side. The orientation of the valoneoyl group of **1** is hence the same as that in rugosin A (**7**).[1]

These structural assignments were confirmed by partial hydrolysis of **1** in hot water, which afforded **7** and tellimagrandin I (**8**).[5,7] The coupling constant (8 Hz) of each anomeric proton of **1** indicated that the acyloxy groups on the two anomeric centers are both β-oriented. Structure **1**, in which the carboxyl group of **7** is esterified with the β-oriented anomeric hydroxyl group of **8**, was thus assigned for rugosin D.

Rugosin E (**2**), a light-brown powder, showed the $[M+Na]^+$ ion peak at m/z 1745 in the FAB-MS, which is consistent with its dimeric molecular formula $C_{75}H_{54}O_{48}$. Duplication of each signal in the ^{1}H-NMR spectrum (500 MHz, in acetone-d_6 + D_2O) showed that **2** is a mixture of two anomers. The chemical shifts of the anomeric protons of each anomer of **2** [δ 6.08, 5.51 (α-anomer); 6.08, 5.04 (β-anomer) ($\alpha:\beta=3:2$)] indicated that one of the two anomeric centers in **2** is acylated and the other is free. Along with the signals of two glucose cores (see Table I), those of four galloyl groups [δ 7.05, 7.01, 7.00, 6.95 (α-anomer); 7.04, 7.01, 6.95, 6.95 (each s, β-anomer) (each s)], a valoneoyl group and an HHDP group [δ 7.14 (Val H_C), 6.63 (HHDP H_B), 6.47, 6.46 (Val H_A and HHDP H_A), 6.18 (Val H_B) (α-anomer); 7.13 (Val H_C), 6.63 (HHDP H_B), 6.47, 6.45 (Val H_A and HHDP H_A), 6.17 (Val H_B) (β-anomer)] were observed. The positive Cotton effect, in the short-wavelength region ($[\theta]_{224}+2.3\times10^5$) of the CD spectrum of **2**, indicated[4] that both the valoneoyl and HHDP groups have the (*S*)-configuration.

The large difference in the chemical shifts of the two protons on C-6 of each glucose core of **2** [$\Delta\delta$ 1.47 (glucose L) and 1.52 (glucose R), α-anomer; $\Delta\delta$ 1.48 (glucose L) and 1.46 (glucose R), β-anomer] indicated that the two HHDP residues (including the HHDP moiety of the valoneoyl group) are on O-4—O-6 of the two glucose cores. Then, the five galloyl residues (including the galloyl moiety of valoneoyl group) are on O-1, O-2 and O-3 of a glucose core and on O-2 and O-3 of another glucose core. The close similarity of the pattern of the glucose carbon signals in the ^{13}C-NMR spectrum (100.6 MHz, in acetone-d_6) of **2** (see Experimental) to that of **6** plus **8**[9] (except for C-1 of **8**)[10] also substantiates these locations of the acyl groups. The notable upfield shift of C-1 of one of the two glucose cores (glucose core L, see formula **2**), relative to the corresponding signal of **6** [δ 93.8 (**6**, C-1)→93.1 (**2**, C-1 of glucose L)], indicates that the galloyl moiety of the valoneoyl group is



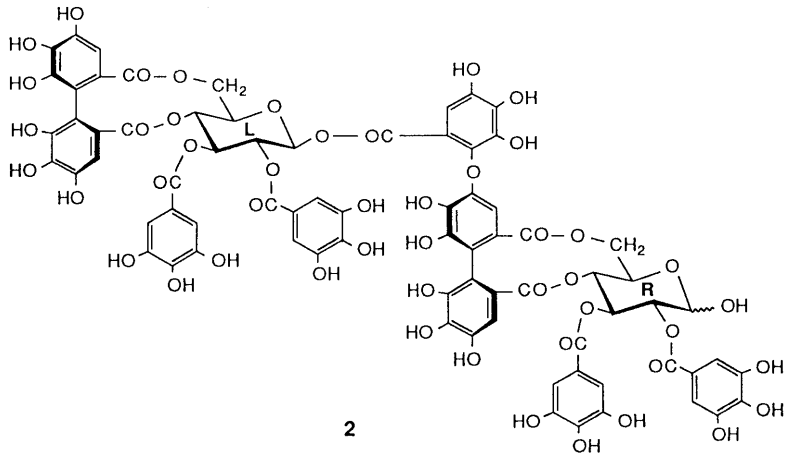


Chart 1

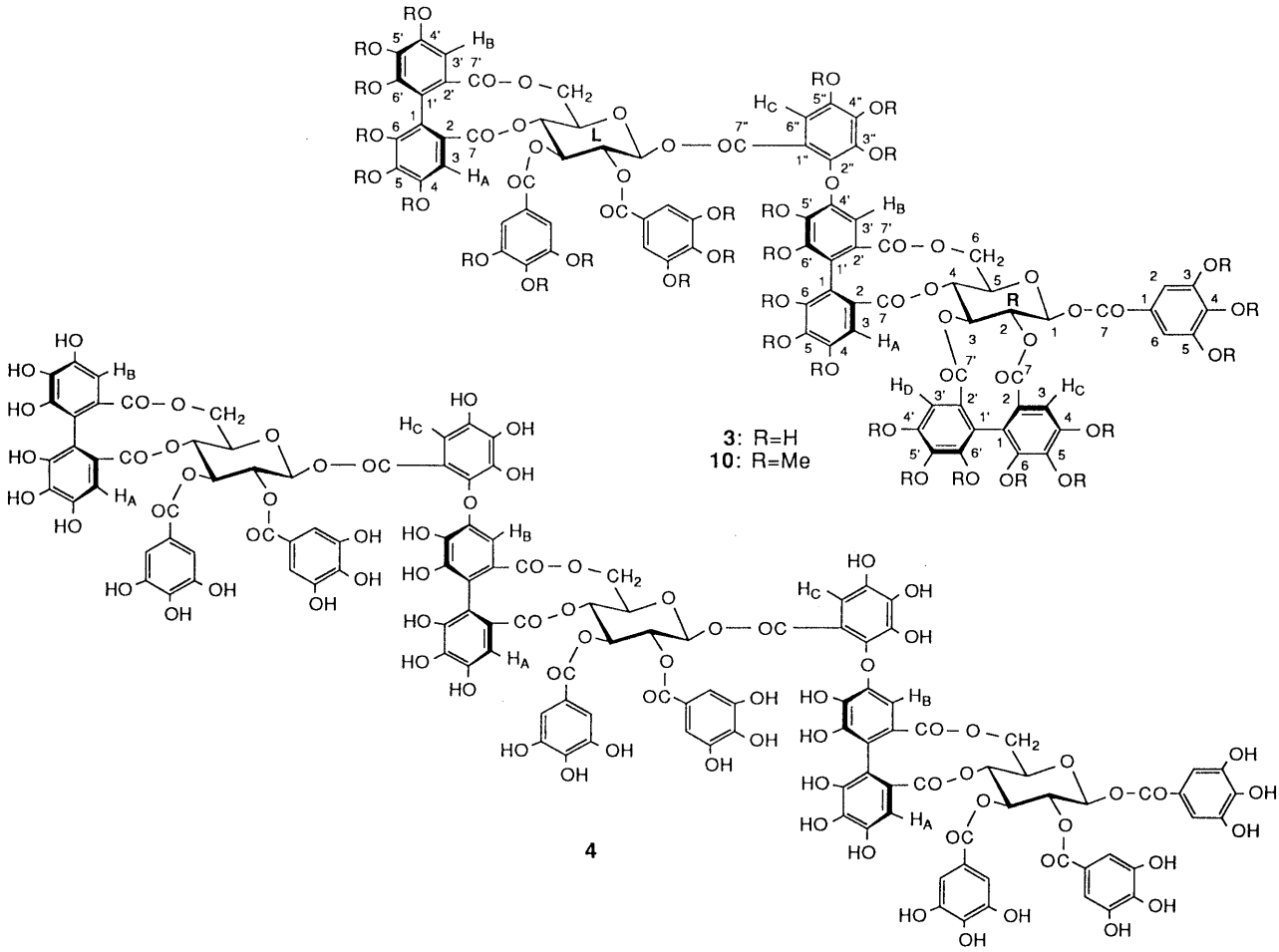
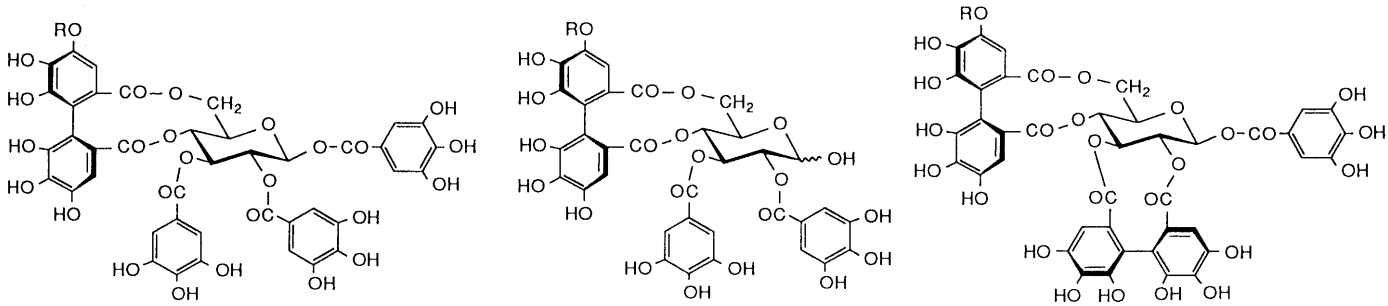


Chart 2



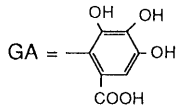


Chart 3

on the anomeric center of this glucose core, as in **1**.

The remarkable upfield shifts of the H_B signal of the valoneoyl group of each anomer [δ 6.18 (α-anomer), 6.17 (β-anomer)] in **2**, relative to one of the two HHDP protons (on the glucose O-6 side) of each anomer of **8** [δ 6.68 (α-anomer), 6.69 (β-anomer)],[1] shows that the orientation of the valoneoyl group in **2** is the same as that in **8**.[1]

Partial hydrolysis of **2** in hot water afforded **8** and rugosin B (**9**).[1] The coupling constant (8 Hz) of H-1, on the acylated anomeric center of each anomer of **2**, indicated that the acyloxy group on this anomeric center is β-oriented. Structure **2**, in which the carboxyl group of **9** is esterified

with the β-oriented anomeric hydroxyl group of **8**, was hence assigned for rugosin E.

Rugosin F (**3**), a light-brown powder, is a dimeric hydrolyzable tannin of molecular formula $C_{82}H_{56}O_{52}$, as indicated by the $[M+Na]^+$ ion peak at *m/z* 1895 in its FAB-MS. The ^{1}H-NMR spectrum (500 MHz, in acetone-d_6+D_2O) showed the presence of three galloyl groups [δ 7.14, 6.99 and 6.95 (2H each, s)], two HHDP groups and a valoneoyl group [δ 7.11 (Val H_C), 6.63 (HHDP H_B), 6.52 (Val H_A), 6.46, 6.44 (HHDP H_A and H_C), 6.40 (HHDP H_D) and 6.20 (Val H_B) (1H each, s)], along with two β-D-glucopyranose cores (see Table I). The CD spectrum of **3** showed a broad positive peak in the short-wavelength region ($[\theta]_{227}+2.6\times10^5$, $[\theta]_{235}+2.5\times10^5$), indicating that all of the HHDP and valoneoyl groups in **3** have the (*S*)-configuration. Methylation of **3** afforded the nonacosa-*O*-methyl derivative **10**.

The chemical shifts of the glucose protons of **3** indicated that all the hydroxyl groups on the two glucopyranose cores are acylated. The large differences of the chemical shifts of the two protons on C-6, in each of these glucose cores ($\Delta\delta$ *ca.* 1.5), indicate that two of the three HHDP residues (including the HHDP moiety of the valoneoyl group) in **3** are on O-4—O-6 of the two glucose cores. The upfield shifts of H-2 (δ 5.14) and H-3 (δ 5.41) of one of the two glucose cores, relative to the corresponding protons of the other glucose core (H-2, δ 5.52; H-3, δ 5.77), indicated[1] that the third HHDP residue is on O-2—O-3 of this glucose core. Therefore, rugosin F is a dimeric tannin composed of casuarictin (**11**)[7] and **6**. The chemical shifts of glucose carbon signals of **3** (see Experimental) are similar to those of **11**[8] plus **6** (except for C-1 of **6**), and substantiate the above-described structural assignment. However, C-1 of one of the two glucose cores in **3** (δ 93.4) showed a slight upfield shift, relative to the corresponding carbon of **6** (δ 93.8). The galloyl residue of the valoneoyl group in **3**, hence, is on O-1 of the glucose core having the acyl groups arranged analogously to **6** (glucose L in formula **3**).

Partial degradation of **3** in hot water afforded **8** and rugosin C (**12**).[1] The chemical shifts of two anomeric protons [δ 6.16 (d, $J=8.5$ Hz) and 6.08 (d, $J=8$ Hz)] indicated that each anomeric center in **3** has a β-oriented acyloxy group. The structure **3**, in which the carboxyl group in **12** is esterified with the β-oriented anomeric hydroxyl group in **8**, was therefore assigned for rugosin F. The production of **12**, upon partial degradation, also indicated that the orientation of the valoneoyl group in **3** is the same as that in **12**.[1]

Rugosin G (**4**) forms a light-brown powder. Its retention volume on high-performance size exclusion chromatography[11] indicated that it is a trimeric hydrolyzable tannin. The ^{1}H-NMR spectrum of this tannin (200 MHz, in acetone-d_6) showed the signals of seven galloyl groups (δ 7.15, 7.03, 7.02, 7.01, 7.01, 7.00 and 6.98), two HHDP groups and a valoneoyl group [δ 7.15 (Val H_C), 7.14 (Val H_C), 6.68 (HHDP H_B), 6.48, 6.47 (2H) (Val $H_A\times2$ and HHDP H_A), 6.23 (Val H_B) and 6.22 (Val H_B)], and also three β-D-glucopyranose cores [δ 6.19, 6.11, 6.08 (each d, $J=8$ Hz, H-1); 5.62, 5.58, 5.54 (dd, $J=8$, 10 Hz, H-2); 5.85, 5.78, 5.77 (each t, $J=10$ Hz, H-3); 5.17, 5.16, 5.10 (each t, $J=10$ Hz, H-4); 4.53, 4.47, 4.43 (each dd, $J=6.5$, 10 Hz, H-5); 5.32, 5.31, 5.27 (each dd, $J=6.5$, 13.5 Hz, H-6); 3.79, 3.76, 3.70 (each d, $J=13.5$ Hz, H-6)]. The CD spectrum of **4** showed a positive Cotton effect in the short-wavelength region ($[\theta]_{224}+3.5\times10^5$). The amplitude of this Cotton effect was comparable to the sum of those of **1** and **7** ($[\theta]_{224}+1.6\times10^5$),[1] indicating the (*S*)-configuration of all of the valoneoyl and HHDP groups.

The chemical shifts of glucose protons in the ^{1}H-NMR spectrum of **4** indicated that all the hydroxyl groups on the two glucopyranose cores are acylated. The large difference in the chemical shifts of the two protons on C-6 of each glucose core ($\Delta\delta$ 1.5—1.6), indicated that the three HHDP residues (including the HHDP moieties of the two valoneoyl groups) are on O-4—O-6 of the three glucose cores. The nine galloyl residues (including the galloyl moieties of the two valoneoyl groups) are hence on O-1, O-2 and O-3 of the three glucose cores. This tannin is accordingly composed of three molecules of **6**. The H_B signals (δ 6.23 and 6.22) of the two valoneoyl groups in **4** are shifted markedly upfield, relative to one of the two HHDP protons (on the glucose O-6 side) of **6** (δ 6.67). The orientation of each valoneoyl group in **4** is therefore the same as that in **7**. The treatment of **4** with hot water afforded **7**, **8** and **9**, in a molar ratio *ca.* 1:1:1. Structure **4** was thus assigned for rugosin G.

Among the oligomeric hydrolyzable tannins of *Rosa rugosa*, rugosins D (**1**) and E (**2**) showed noticeable host-mediated antitumor activity.[12] The former also exhibited anti-herpes simplex virus (HSV) activity.[13] The present investigation on the structures of these tannins, including the orientation of the valoneoyl group(s), is expected to provide a firm basis for the discussion of their structure–activity correlation.

Experimental

Ultraviolet (UV) and infrared (IR) spectra were recorded on a Hitachi 200—10 spectrophotometer and a JASCO A-102 spectrometer, respectively. Optical rotations were measured on a JASCO DIP-4 digital polarimeter. CD spectra were recorded on a JASCO J-20 spectrometer. Electron impact (EI) mass spectra were recorded on a Shimadzu LKB-9000 instrument. FAB-MS were recorded on a VG 70-SE spectrometer, or a JEOL GMS HX-100 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded with a JEOL FX-200 spectrometer (200 MHz for ^{1}H-NMR and 50.1 MHz for ^{13}C-NMR) in acetone-d_6 or in acetone-d_6+D_2O. Chemical shifts were given in δ values (ppm) from tetramethylsilane. A Hitachi R22-FTS spectrometer (90 MHz for ^{1}H-NMR), a Bruker AM-400 spectrometer (100.6 MHz for ^{13}C-NMR) and a Varian VXR-500 instrument (500 MHz for ^{1}H-NMR and 125.7 MHz for ^{13}C-NMR) were also used for measurements of ^{1}H- and ^{13}C-NMR spectra. High-performance liquid chromatography (HPLC) was performed on a LiChrosorb RP-18 (10 μm) column (4 × 250 mm) with 0.1 M H_3PO_4–0.1 M KH_2PO_4–EtOH–ethyl acetate (50:50:6:5, v/v), in a Shimadzu CTO-1 oven at 40 °C. The flow rate was set at 1.1 ml, and the eluate was monitored with a Shimadzu UVD-1 detector (254 nm). Light petroleum refers to the fraction boiling in the range of 85—120 °C.

Isolation of Rugosins D—G from Flower Petals of *Rosa rugosa* A portion (4.9 g) of the ethyl acetate extract[1] (28.8 g), which was obtained from the 70% acetone homogenate of dried flower petals (280 g) of *Rosa rugosa*, collected at Ishikari-hama, Hokkaido, was chromatographed over Sephadex LH-20 with MeOH–70% aqueous acetone (20:0→20:1→20:2→20:4, v/v), to give rugosins E (**2**) (109 mg), D (**1**) (486 mg), F (**3**) (110 mg) and G (**4**) (32 mg).

Rugosin D (1) A light-brown powder, $[\alpha]_D+118°$ ($c=1$, acetone). *Anal.* Calcd for $C_{82}H_{58}O_{52}\cdot9H_2O$: C, 48.34; H, 3.76. Found: C, 48.31; H, 3.64. FAB-MS *m/z*: 1875 $[M+H]^+$, 1897 $[M+Na]^+$. UV λ_{max}^{MeOH} nm (log ε): 219 (5.17), 277 (4.84). IR ν_{max}^{KBr} cm^{-1}: 1730, 1620. CD (MeOH): $[\theta]_{225}+2.5\times10^5$, $[\theta]_{258}-3.8\times10^4$, $[\theta]_{280}+8.1\times10^4$. ^{1}H-NMR: see the text and Table I. ^{13}C-NMR (125.7 MHz, in acetone-d_6) δ: 62.9, 63.0 [Glc(L) (glucose L in formula **1**) C-6, Glc(R) (glucose R in formula **1**) C-6], 70.5,

70.6 [Glc(L) C-4, Glc(R) C-4], 71.7 (2C) [Glc(L) C-2, Glc(R) C-2], 72.8, 72.9 [Glc(L) C-5, Glc(R) C-5], 73.1, 73.2 [Glc(L) C-3, Glc(R) C-3], 93.1 [Glc(L) C-1], 93.5 [Glc(R) C-1], 105.0 (Val C-3′), 107.6, 107.8 (HHDP C-3, Val C-3), 108.1 (HHDP C-3′), 110.0 (Val C-6″), 110.0 (2C), 110.1 (6C), 110.3 (2C) [galloyl (Gall) C-2 × 5, C-6 × 5], 112.7 (Val C-1″), 115.6 (HHDP C-1′), 115.7, 115.7 (Val C-1, HHDP C-1), 117.7 (Val C-1′), 119.6, 120.0, 120.1, 120.3, 120.3 (Gall C-1 × 5), 125.3, 125.7, 125.8, 126.4 (Val C-2, C-2′, HHDP C-2, C-2′), 136.4 (HHDP C-5′), 136.6, 136.7 (Val C-5, HHDP C-5), 137.2 (Val C-5′), 137.7 (Val C-2″), 139.2 (2C), 139.4, 139.5, 139.8 (Gall C-4 × 5), 140.6 (Val C-3″), 141.1 (Val C-4″), 143.3 (Val C-5″), 144.3, 144.4 (HHDP C-6, C-6′), 144.6, 144.8 (Val C-6, C-6′), 145.2, 145.2 (2C), 145.2 (HHDP C-4, C-4′, Val C-4), 145.7 (2C), 145.8 (2C), 145.9 (2C), 145.9 (2C), 146.1 (2C) (Gall C-3 × 5, C-5 × 5), 146.4 (Val C-4′), 162.4 (Val C-7″), 164.9 [Gall (at O-1 of glucose R) C-7], 165.7, 165.7 [Gall (at O-2 of glucose L) C-7, Gall (at O-2 of glucose R) C-7], 166.3 (2C) [Gall (at O-3 of glucose L) C-7, Gall (at O-3 of glucose R)], 167.6 (HHDP C-7), 167.7 (Val C-7), 167.8 (Val C-7′), 168.0 (HHDP C-7′).

Rugosin E (2) A light-brown powder, $[\alpha]_D$ +140° (c=1, acetone). *Anal.* Calcd for $C_{75}H_{54}O_{48}\cdot 5H_2O$: C, 49.68; H, 3.56. Found: C, 49.78; H, 3.27. FAB-MS *m/z*: 1745 ([M+Na]$^+$). UV λ_{max}^{MeOH} nm (log ε): 220 (5.19), 275 (4.87). IR ν_{max}^{KBr} cm^{-1}: 1730, 1620. CD (MeOH): $[\theta]_{224}$ +2.3 × 10^5, $[\theta]_{258}$ −5.0 × 10^4, $[\theta]_{282}$ +9.7 × 10^4. ^{1}H-NMR: see the text and Table I. ^{13}C-NMR (100.6 MHz, in acetone-d_6) δ: 62.9 [Glc(L) (glucose L in formula **2**) C-6], 63.4 [Glc(R) (glucose R in formula **2** C-6, α- and β-anomers], 66.7 [Glc(R) C-5, α-anomer], 70.5 [Glc(L) C-4], 71.0 [Glc(R) C-4, α- and β-anomers], 71.2 [Glc(R) C-3, α-anomer], 71.6 [Glc(L) C-2], 71.7 [Glc(R) C-5, β-anomer], 72.8 [Glc(L) C-5; Glc(R) C-2, α-anomer], 73.1 [Glc(L), C-3], 73.5 [Glc(R) C-3, β-anomer], 74.0 [Glc(R) C-2, β-anomer], 91.1 [Glc(R) C-1, α-anomer], 93.1 [Glc(L) C-1], 96.5 [Glc(R) C-1, β-anomer], 105.1 (Val C-3′), 107.6, 107.7 (HHDP C-3, Val C-3), 108.2 (HHDP C-3′), 109.8 (Val C-6″), 110.1 (8C) (Gall C-2 × 4, C-6 × 4), 112.9 (Val C-1″), 115.6 (3C) (HHDP C-1, C-1′, Val C-1), 117.6 (Val C-1′). 120.0, 120.1, 120.2, 120.3, 120.5, 120.5, 120.7, 120.9 (Gall C-1 × 4), 125.5, 125.6, 125.9, 126.3 (Val C-2, C-2′, HHDP C-2, C-2′), 136.3, 136.4 (2C) (HHDP C-5, C-5′, Val C-5), 137.0 (Val C-5′), 137.6 (Val C-2″), 138.9, 139.0, 139.1, 139.3 (Gall C-4 × 4), 140.3 (Val C-3″), 140.9 (Val C-4″), 143.2 (Val C-5″), 144.2 (2C) (HHDP C-6, C-6′), 144.5, 144.6 (Val C-6, C-6′), 145.0 (3C) (HHDP C-4, C-4′, Val C-4), 145.6 (4C), 145.8 (4C) (Gall C-3 × 4, C-5 × 4), 146.2, 146.3 (Val C-4′), 162.3 (Val C-7″), 164.9 [Gall (at O-1 of glucose R) C-7], 165.7 [Gall (at O-2 of glucose L) C-7, Gall (at O-2 of glucose R, β-anomer) C-7], 166.2 [Gall (at O-3 of glucose L) C-7, Gall (at O-2 of glucose R, α-anomer) C-7], 166.3 [Gall (at O-3 of glucose R, β-anomer) C-7], 166.5 [Gall (at O-3 of glucose R, α-anomer) C-7], 167.5 (HHDP C-7), 167.6 (Val C-7), 167.9, 168.0 (Val C-7′, HHDP C-7′).

Rugosin F (3) A light-brown powder, $[\alpha]_D$ +88° (c=1, acetone). *Anal.* Calcd for $C_{82}H_{56}O_{52}\cdot 12H_2O$: C, 47.14; H, 3.86. Found: C, 47.33; H, 3.75. FAB-MS *m/z*: 1895 ([M+Na]$^+$). UV λ_{max}^{MeOH} nm (log ε): 218 (5.18), 273 (4.85). IR ν_{max}^{KBr} cm^{-1}: 1730—1710, 1610. CD (MeOH): $[\theta]_{227}$ +2.6 × 10^5, $[\theta]_{235}$ +2.5 × 10^5, $[\theta]_{260}$ −6.5 × 10^4, $[\theta]_{281}$ +5.2 × 10^4. ^{1}H-NMR: see the text and Table I. ^{13}C-NMR (50.1 MHz, in acetone-d_6) δ: 63.2 [Glc(L) (glucose L in formula **3**) C-6, Glc(R) (glucose R in formula **3**) C-6], 69.3 [Glc(R) C-4], 70.7 [Glc(L) C-4], 71.9 [Glc(L) C-2], 73.1 [Glc(L) C-5], 73.5 (2C) [Glc(L) C-3), Glc(R) C-5], 74.9 [Glc(R) C-2], 77.2 [Glc(R) C-3], 92.3 [Glc(R) C-1], 93.4 [Glc(L) C-1], 105.6 (Val C-3′), 107.4 (2C), 107.5, 108.0 (HHDP C-3 × 2, C-3′, Val C-3), 108.4 (HHDP C-3′), 110.1—110.4 (7C) (Val C-6″, Gall C-2 × 3, C-6 × 3), 113.4 (Val C-1″), 114.3, 114.9, 115.0, 115.8 (2C) (HHDP C-1 × 2, C-1′ × 2, Val C-1), 117.7 (Val C-1′), 120.1, 120.4, 120.7 (Gall C-1 × 3), 125.6, 126.0, 126.1, 126.2, 126.6 (2C) (Val C-2, C-2′, HHDP C-2 × 2, C-2′ × 2), 136.3, 136.6 (3C), 136.8 (HHDP C-5 × 2, C-5′ × 2, Val C-5), 137.3 (Val C-5′), 137.8 (Val C-2″), 139.2, 139.4, 139.9 (Gall C-4 × 3), 140.6 (Val C-3″), 141.0 (Val C-4″), 143.4 (Val C-5″), 144.4 (4C) (HHDP C-6 × 2, C-6′ × 2), 144.8, 144.9 (Val C-6, C-6′), 145.2 (2C), 145.3 (2C), 145.4 (HHDP C-4 × 2, C-4′ × 2, Val C-4), 145.8 (2C), 145.9 (2C), 146.3 (2C) (Gall C-3 × 3, C-5 × 3), 146.6 (Val C-4′), 162.7 (Val C-7″), 164.9 [Gall (at O-1 of glucose L) C-7], 165.7, 165.7 [Gall (at O-2 of glucose L) C-7], 166.3 [Gall (at O-3 of glucose L], 167.6 [HHDP (at O-4—O-6 of glucose L) C-7], 167.8 (2C) (Val C-7, Val C-7′), 168.0 [HHDP (at O-4—O-6 of glucose L) C-7′], 168.7 [HHDP (at O-2—O-3 of glucose R) C-7], 169.1 [HHDP (at O-2—O-3 of glucose R) C-7′].

Methylation of Rugosin D (1) and Rugosin F (3) Dimethyl sulfate (48 μl) and potassium carbonate (100 mg) were added to a solution (1.2 ml) of **1** (20 mg) in acetone. The mixture was stirred for 24 h at room temperature, and then refluxed for 12 h. It was centrifuged to remove the insoluble material, and the solvent of the supernatant was evaporated off. The residue was subjected to preparative thin layer chromatography (TLC) [Kieselgel 60 PF_{254}, light petroleum–dichloromethane–acetone, 4 : 6 : 3, v/v], to give nonacosa-*O*-methylrugosin D (**5**) (11 mg). An analogous treatment of **3** (22 mg) afforded its nonacosa-*O*-methyl derivative (**10**) (10 mg).

Nonacosa-*O*-methylrugosin D (5) Colorless powder, $[\alpha]_D$ +52° (c=1, acetone). *Anal.* Calcd for $C_{111}H_{116}O_{52}\cdot H_2O$: C, 57.96; H, 5.17. Found: C, 57.70; H, 5.00. EI-MS *m/z*: 646, 614, 570 [octa-*O*-methylvaloneoyl (OMV)], 436, 422, 404, 360 [hexamethoxydiphenoyl (HMDP)], 212, 197, 195 [tri-*O*-methylgalloyl (TMG)]. ^{1}H-NMR (500 MHz, in acetone-d_6) δ: 7.34 (2H, s) (TMG), 7.24 (3H, s) (TMG, OMV, H_C), 7.23, 7.23, 7.18 (2H each, s) (TMG × 3), 6.92, 6.79, 6.76, 6.60 (1H each, s) (OMV H_A, H_B; HMDP H_A × 2, H_B × 2), 6.28, 6.28 (1H each, d, J=8 Hz) (Glc H-1 × 2), 5.94, 5.89 (1H each, t, J=9.5 Hz) (Glc H-3 × 2), 5.65, 5.58 (1H each dd, J=8, 9.5 Hz) (Glc H-2 × 2), 5.30, 5.23 (1H each, t, J=10 Hz) (Glc H-4 × 2), 5.30, 5.28 (1H each, dd, J=6.5, 13.5 Hz) (Glc H-6 × 2), 4.64, 4.61 (1H each, br dd, J=6.5, 10 Hz) (Glc H-5 × 2), 4.02 (3H, s, OMe), 3.94 (1H, d, J=13.5 Hz) (Glc H-6), 3.91—3.63 (28 × OMe). The signal of one of the two protons on C-6 of a glucose core is overlapped by the methoxyl signals.

Nonacosa-*O*-methylrugosin F (10) Colorless powder, $[\alpha]_D$ +26° (c=1, acetone). *Anal.* Calcd for $C_{111}H_{114}O_{52}\cdot 2H_2O$: C, 57.56; H, 5.13. Found: C, 57.64; H, 4.97. EI-MS *m/z*: 646, 614, 570 (OMV), 436, 422, 404, 360 (HMDP), 212, 197, 195 (TMG). ^{1}H-NMR (200 MHz, in acetone-d_6) δ: 7.34, 7.24, 7.19 (2H each, s) (TMG × 3), 7.23 (1H, s) (OMV H_C), 6.95, 6.85, 6.81, 6.77, 6.69 (1H each, s), 6.61 (2H, s) (OMV H_A, H_B; HMDP H_A, H_B, H_C, H_D), 6.29 (1H, d, J=8 Hz) (Glc H-1), 6.26 (1H, d, J=8.5 Hz) (Glc H-1), 5.90 (1H, t, J=9.5 Hz) (Glc H-3), 5.57 (1H, dd, J=8, 9.5 Hz) (Glc H-2), 5.52 (1H, t, J=9.5 Hz) (Glc H-3), 5.31 (1H, dd, J=6.5, 13.5 Hz) (Glc H-6), 5.27 (1H, dd, J=6.5, 13.5 Hz) (Glc H-6), 5.24 (1H, t, J=10 Hz) (Glc H-4), 5.19 (1H, dd, J=8.5, 9.5 Hz) (Glc H-2), 5.09 (1H, t, J=10 Hz) (Glc H-4), 4.60 (1H, br dd, J=6.5, 10 Hz) (Glc H-5), 4.52 (1H, br dd, J=6.5, 10 Hz) (Glc H-5), 4.06 (3H, s, OMe), 3.94—3.63 (28 × OMe). The signal of one of the two protons on C-6 of each glucose core is overlapped by the methoxyl signals.

Partial Hydrolysis of Rugosins D (1), E (2) and F (3) An aqueous solution (2 ml) of **1** (25 mg) in a sealed tube was heated in a boiling-water bath for 1.5 h, and then the solvent was evaporated off. The residue was dissolved in MeOH, and chromatographed over Sephadex LH-20 with MeOH as the developer, to give tellimagrandin I (**8**) (6.7 mg) and rugosin A (**7**) (3.3 mg), which were identified by ^{1}H-NMR. An aqueous solution (2 ml) of **2** (23 mg) was treated with hot water, and the products were separated by preparative TLC (Avicel SF, H_2O), to give **8** (5.4 mg) and rugosin B (**9**) (3.0 mg). An analogous treatment of **3** (26 mg) afforded **8** (5.5 mg) and rugosin C (**12**) (3.4 mg).

Rugosin G (4) A light-brown powder, $[\alpha]_D$ +109° (c=1, acetone). *Anal.* Calcd for $C_{123}H_{86}O_{78}\cdot 18H_2O$: C, 47.11; H, 3.92. Found: C, 47.17; H, 3.81. UV λ_{max}^{MeOH} nm (log ε): 218 (5.31), 276 (5.05). IR ν_{max}^{KBr} cm^{-1}: 1730—1710, 1610. CD (MeOH): $[\theta]_{224}$ +3.5 × 10^5, $[\theta]_{258}$ −6.1 × 10^4, $[\theta]_{280}$ +1.3 × 10^5. ^{1}H-NMR: see text.

Molecular Weight Estimation of Rugosin G (4) by Size Exclusion Chromatography High-performance size exclusion chromatography was performed on a Shimadzu HSG-15 column (7.9 mm × 50 cm) at 40 °C with tetrahydrofuran as the eluant. Plots of the retention volumes (v_R, in ml) of **4**, **1**(dimer) and **6** (monomer), against the logarithms of their molecular weights (MW), showed a linear relationship: $\log MW = -0.41 \times v_R + 7.97$.

Quantitative Analysis of Hydrolyzates of Rugosin G (4) An aqueous solution (1 ml) of **4** (1 mg) was heated in a boiling-water bath for 2.5 h, and the hydrolysis of **4** was monitored by HPLC, revealing the production of **7** [t_R (retention time) 10.1 min], **8** (t_R 2.5 and 3.4 min)[14] and **9** (t_R 3.1 and 4.2 min) in a molar ratio of *ca.* 1 : 1 : 1. Production and degradation of **2** (t_R 9.2 and 13.9 min)[14] during this hydrolysis were also observed.

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References and Notes

1) For Part VIII, see T. Hatano, N. Ogawa, T. Yasuhara and T. Okuda, *Chem. Pharm. Bull.*, **38**, 3308 (1990).

2) T. Okuda, T. Yoshida and T. Hatano, *Heterocycles*, **30**, 1195 (1990).
3) For a preliminary communication, see T. Okuda, T. Hatano and N. Ogawa, *Chem. Pharm. Bull.*, **30**, 4234 (1982).
4) T. Okuda, T. Yoshida, T. Hatano, T. Koga, N. Toh and K. Kuriyama, *Tetrahedron Lett.*, **23**, 3937 (1982).
5) C. K. Wilkins and B. A. Bohm, *Phytochemistry*, **15**, 211 (1976).
6) T. Okuda, T. Hatano and T. Yasui, *Heterocycles*, **16**, 1321 (1981).
7) T. Okuda, T. Yoshida, M. Ashida and K. Yazaki, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1765.
8) T. Yoshida, T. Hatano, T. Okuda, M. U. Memon, T. Shingu and K. Inoue, *Chem. Pharm. Bull.*, **32**, 1790 (1984).
9) T. Hatano, T. Yoshida, T. Shingu and T. Okuda, *Chem. Pharm. Bull.*, **36**, 2925 (1988).
10) An analogous upfield shift of another signal, δ 67.2 (**8**, C-5, α-anomer)$\rightarrow$66.7 (**2**, C-5 of glucose R, α-anomer), was probably also due to an effect of some steric compression.
11) T. Okuda, T. Yoshida and T. Hatano, *J. Nat. Prod.*, **52**, 1 (1989).
12) K. Miyamoto, N. Kishi, R. Koshiura, T. Yoshida, T. Hatano and T. Okuda, *Chem. Pharm. Bull.*, **35**, 814 (1987).
13) K. Fukuchi, H. Sakagami, T. Okuda, T. Hatano, S. Tanuma, K. Kitajima, Y. Inoue, S. Inoue, S. Ichikawa, M. Nonoyama and K. Konno, *Antiviral Res.*, **11**, 285 (1989).
14) Hydrolyzable tannins forming anomer mixtures often show dual or multiple peaks. See, T. Hatano, T. Yoshida and T. Okuda, *J. Chromatogr.*, **435**, 285 (1988).