Tannins and Related Compounds. CVI.[1] Preparation of Aminoalditol Derivatives of Hydrolyzable Tannins Having α- and β-Glucopyranose Cores, and Its Application to the Structure Elucidation of New Tannins, Reginins A and B and Flosin A, Isolated from *Lagerstroemia flos-reginae* RETZ.

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To avoid tautomerism in the hydrolyzable tannins which lack an acyl group at the glucose C-1 position, a new method for the protection of the C-1 atom has been developed. That is reaction of the tannins with *p*-anisidine in the presence of acetic acid, followed by sodium cyanoborohydride reduction, afforded, without notable hydrolysis of ester bonds, the aminoalditol derivatives (1a—7a) in 50—80% yields. The proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectra of these derivatives exhibited much simpler signal patterns typical of an open-chain form of glucose, and almost all the signals could be assigned.

Application of this method to the structure elucidation of the new tannins, flosin A (22) and reginins A (23) and B (24), isolated from the leaves of *Lagerstroemia flos-reginae* RETZ. (Lythraceae), established their structures including the orientation of the 4,6-positioned valoneoyl group. In addition, the structure of a new hydrolyzable tannin, lagerstroemin (21), which was concomitantly isolated from the above species, was elucidated.

Keywords hydrolyzable tannin; aminoalditol derivative; reginin A; reginin B; flosin A; lagerstroemin; valoneic acid; *Lagerstroemia flos-reginae*; Lythraceae; tannin

Whilst considerable progress has been made on elucidation of the chemistry and structures of hydrolyzable tannins by employing proton and carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectroscopic techniques, elucidation of the structures of hydrolyzable tannins based on a mixture of α- and β-glucopyranose cores has been severely hampered by the complexty of the signal patterns. In particular, when these tautomeric isomers exist in almost equal proportions, discrimination of signals arising from the α- and β-anomers is difficult from the signal intensities, and therefore the assignment of each signal is difficult. Moreover, in the cases of dimeric and trimeric hydrolyzable tannins having no acyl groups at the glucose C-1 position(s), the spectra are even more complicated owing to the occurrence of many tautomeric isomers. To overcome these difficulties, we have made several attempts to prepare derivatives in which tautomerism can not occur, and we found that reaction of these tannins with *p*-anisidine in ethanolic acetic acid, followed by sodium cyanoborohydride reduction,[2] affords, without notable hydrolysis of ester bonds, aminoalditol derivatives in relatively high yields. The ^{1}H- and ^{13}C-NMR spectra of these derivatives were found to be extremely simplified, showing signal patterns typical of an open-chain form of glucose. Subsequently, we have applied this method to the structure elucidation of a monomeric (flosin A) and two dimeric hydrolyzable tannins (reginins A and B) isolated from the Indonesian medicinal plant, *Lagerstroemia flos-reginae* RETZ. (Lythraceae), and unequivocally determined their structures, including the orientation of the valoneic acid ester group. This paper first describes the method for preparing aminoalditol derivatives of several structurally known hydrolyzable tannins and next deals with the structure elucidation of tannins in *L. flos-reginae*, together with their isolation.

Preparation of Aminoalditol Derivatives Many methods to protect the carbohydrate C-1 position have been reported,[3] but most of them are not applicable to the hydrolyzable tannins because of their instability to acids and bases. Formation of an *O*-alkyl ether or an *O*-acyl ester under mild conditions seems to be a simple and convenient method for the protection of the anomeric hydroxyl group, but separation of the α- and β-anomers produced is usually very difficult. We noticed that primary amines readily react with the carbohydrate C-1 atom in a weakly acidic medium to form a glycosyl amine,[2] and among various amines (monomethyl amine, benzylamine, aniline and *p*-anisidine) tested, *p*-anisidine was found to be the most satisfactory. Subsequent reduction with sodium cyanoborohydride afforded, without notable hydrolysis of the ester linkage, the aminoalditol derivatives in relatively high yields. The ^{1}H-NMR data for the aminoalditol derivatives (**1a—7a**) prepared from pedunculagin (**1**),[4] praecoxin A (**2**),[5] rugosin B (**3**),[5] camelliin A (**4**),[6] 1-desgalloyleugeniin (**5**),[7] gemin D (**6**)[8] and rugosin E (**7**)[9] are listed in Table I.

As is evident from this table, almost all the aminoalditol signals could be assigned unambiguously. It was found that among these signals, the H-3 signal invariably appears at the lowest magnetic field, whereas the H-1 methylene signals appear at the highest position (δ 3.3—3.7) as the AB-portions of typical ABX-type splitting patterns. The aromatic signals arising from the anisidine moiety were always observed as a four-proton singlet which was readily distinguishable from other aromatic signals, and from this signal coupled with the methoxyl signal, the number of

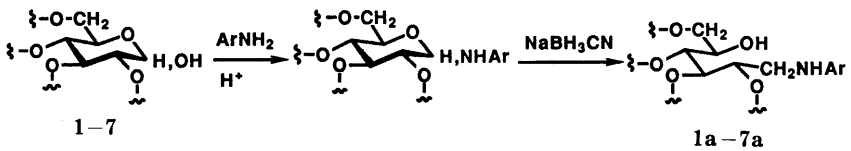


Chart 1

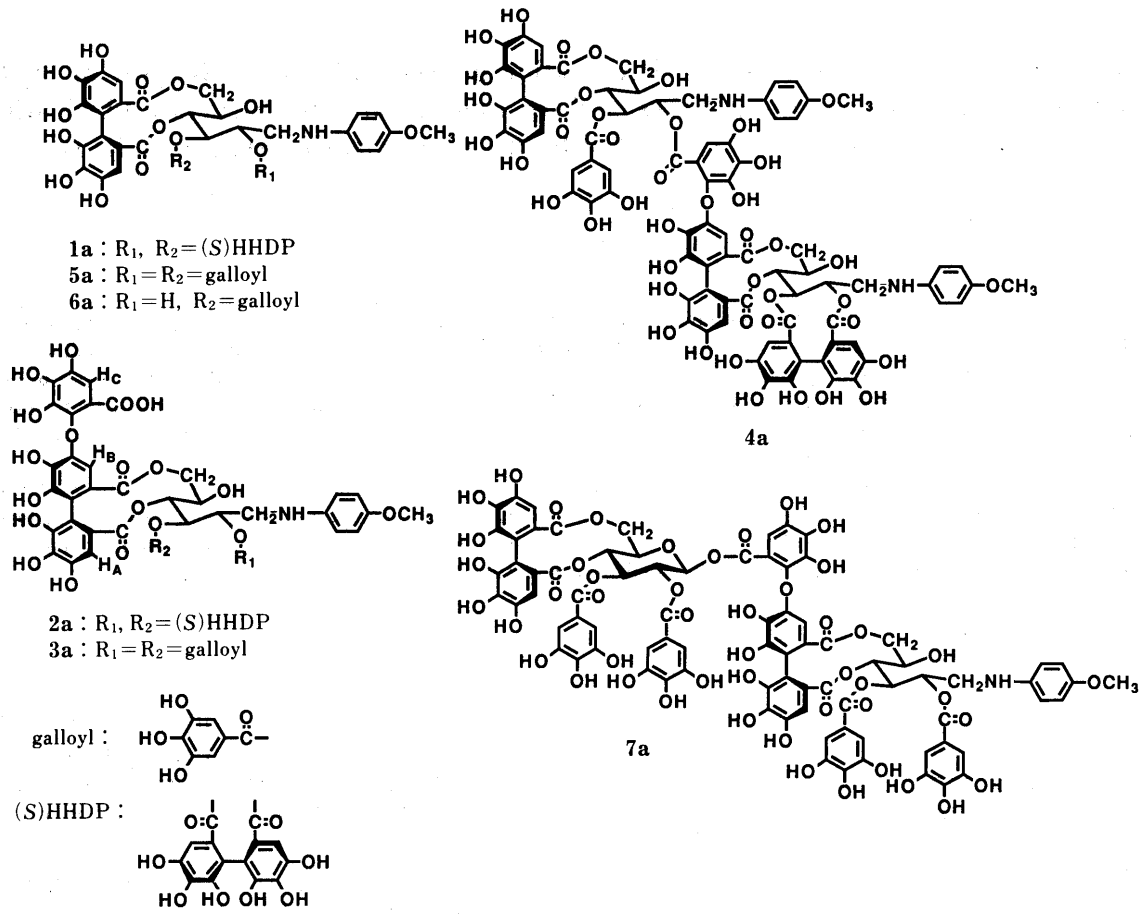


Chart 2

TABLE I. ^{1}H-NMR Spectral Data for Compounds **1a**, **2a**, **3a**, **4a**, **5a**, **6a**, **7a**, **22a**, **23a** and **24a**

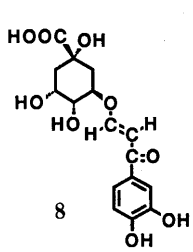
		23a	**24a**[a,c]	**22a**[a,c]	**1a**[b]	**2a**[a]	**3a**[b]	**4a**[a,d]	**5a**[b]	**6a**[b]	**7a**[a,c]
4,6-HHDP	H_A	6.66		6.89	6.68	6.68	6.80	6.68	6.85	6.60	6.71
or valoneoyl	H_B	6.55	6.50—6.60[f]	6.63	6.54	6.21	6.15	6.16	6.47	6.53	6.10
	H_C	7.06		7.05		7.15	7.20	6.81			7.10
Aminoalditol	H-1	3.70[e]	3.64[e]	3.65[e]	3.30—3.70[e]	3.68[e]	3.40—3.70[e]	3.50—3.60[e]	3.30—3.70[e]	3.30—3.70[e]	3.30—3.70[e]
moiety		3.44 (dd, J=8, 12)	3.42 (dd, J=8, 15)	3.46 (dd, J=8, 13)		3.46 (dd, J=8, 12)		3.33 (dd, J=9, 13)			
	H-2	5.18 (ddd, J=2,8,9)	5.11 (ddd, J=2, 8, 8)	5.21 (m)	5.28 (m)	5.26 (m)	5.50 (m)	5.11—5.21[e]	5.51 (m)	4.28 (m)	5.54 (m)
	H-3	5.52 (dd, J=2, 9)	5.49 (dd, J=2, 9)	5.55 (dd, J=2, 10)	5.56 (dd, J=2, 10)	5.53 (dd, J=2, 10)	5.84 (t, J=5)	5.38—5.45[e]	5.89 (t, J=5)	5.54 (dd, J=5, 8)	5.86 (t, J=5)
	H-4	5.14 (dd, J=2, 9)	5.04 (dd, J=2, 8)	5.20 (dd, J=2, 8)	5.28 (m)	5.25 (dd, J=2, 8)	5.34 (dd, J=5, 8)	5.11—5.21[e]	5.38 (dd, J=5, 8)	5.38 (dd, J=5, 8)	5.35 (dd, J=5, 8)
	H-5	4.22 (dd, J=3, 9)	4.04 (dd, J=2, 8)	4.22 (dd, J=2, 8)	4.24 (br d, J=8)	4.25 (dd, J=2, 8)	4.05 (br d, J=8)	4.15 (br d, J=8)	4.06 (br d, J=8)	4.20 (dd, J=3, 8)	4.07 (br d, J=8)
	H-6	4.50 (dd, J=3, 12)	4.36 (dd, J=3, 13)	4.63 (dd, J=3, 12)	4.70 (dd, J=3, 13)	4.60 (dd, J=3, 13)	4.60 (dd, J=3, 12)	4.49 (dd, J=3, 13)	4.66 (dd, J=3, 12)	4.60 (dd. J=3, 12)	4.64 (dd, J=3, 12)
		4.02 (d, J=12)	3.69[e]	3.98 (d, J=12)	3.95 (d, J=13)	3.88 (d, J=13)	3.79 (d, J=12)	3.50—4.00[e]	3.83 (d, J=12)	3.88 (d, J=12)	3.82 (d, J=12)
Anisidine		6.71	6.69	6.70	6.69	6.70	6.71	6.58, 6.38	6.74	6.71	6.72
moiety		(4H)	(4H)	(4H)	(4H)	(4H)	(4H)	(4H) (4H)	(4H)	(4H)	(4H)
	OMe	3.68	3.67	3.67	3.66	3.67	3.67	3.45, 3.54	3.67	3.68	3.67

Acetone-d_6 + D_2O, ppm, Hz. *a*) Spectra measured at 270 MHz. *b*) Spectra measured at 100 MHz. *c*) Data for the aminoalditol moiety. *d*) Data for the aminoalditol of the praecoxin A moiety. *e*) Overlapped with other signals. *f*) Individual signals could not be assigned.

anisidino groups could be ascertained. Considering the coupling constants of the aminoalditol signals, substitution at the C-2 and C-3 positions with either a galloyl or a hexahydroxydiphenoyl (HHDP) ester group seems to affect, the conformation of the aminoalditol moiety as a whole. Namely, in the cases of 2,3-galloyl derivatives (**3a**, **5a** and **7a**), the coupling constants of H-2 and H-3 and of H-3 and H-4 were 5 Hz, whereas the 2,3-HHDP derivatives (**1a**, **2a** and **4a**) exhibited a larger coupling constant ($J=8$ Hz) of H-2 and H-3 and a smaller one ($J=2$ Hz) of H-3 and H-4. One of the characteristic features in the spectra of 4,6-valoneoyl derivatives (**2a**, **3a**, **4a** and **7a**) is the observation of the valoneoyl H_B signal at extremely high field (δ 6.10—6.21). This upfield shift was observed only in the compounds where the 'branched' gallic acid moiety (in the valoneoyl group) is attached to the aromatic ring at the glucose C-6 position (*vide infra*).

Isolation of Tannins from *Lagerstroemia flos-reginae* The dried leaves of *L. reginae*, collected in Indonesia, were extracted with aqueous acetone, and the concentrated extract was partitioned between water and ethyl acetate. The aqueous layer was subjected to Sephadex LH-20 chromatography with H_2O containing increasing proportions of methanol to give two fractions. Each fraction was repeatedly chromatographed over Sephadex LH-20, MCI-gel CHP 20P, TSK-gel Toyopearl HW-40F, TSK-gel Phenyl Toyopearl 650 M and various ODS-type gels to yield new tannins named lagerstroemin (**21**), flosin A (**22**) and reginins A (**23**) and B (**24**), together with 3-*O*-caffeoylquinic acid (**8**),[10] gentisic acid 5-*O*-β-D-glucopyranoside (**9**),[11] brevifolin carboxylic acid (**13**),[12] 4,6-(*S*)-HHDP-D-glucose (**11**),[13] pedunculagin (**1**),[4] 2,3-(*S*)-HHDP-D-glucose (**12**),[14] gentisic acid 5-*O*-β-D-(6′-*O*-galloyl)-glucopyranoside (**10**),[11] casuarinin (**15**),[15] casuariin (**14**),[15] stachyurin (**16**),[15] punicacortein A (**20**),[16] 5-desgalloyl stachyurin (**17**),[17] castalagin (**18**)[15] and vescalagin (**19**).[15] The known compounds were identified by direct comparisons of their chemical and physical data with those of authentic samples.

Structure Elucidation of New Tannins (21—24) Lagerstroemin (**21**) showed, in the ^{1}H-NMR spectrum, seven aliphatic proton signals whose chemical shifts and coupling patterns were similar to those of casuarinin (**15**).[15] In the aromatic field, the chemical shifts of three signals (δ 6.83, 6.59 and 6.41) out of six one-proton singlets were also correlated with those of **15**. Methylation of **21** with dimethyl sulfate and potassium carbonate in dry acetone yielded the octadecamethyl ether (**21a**). Subsequent alkaline methanolysis of **21a** gave three products (**21b**, **21c** and **21d**), of which compound **21b** was identified as dimethyl (*S*)-hexamethoxydiphenoate.[18] The ^{1}H-NMR spectrum of **21c** showed three aromatic one-proton singlets and seven methoxyl signals. These facts coupled with the observation of the intense molecular ion peak at m/z 568 in the electron impact mass spectrum (EI-MS) suggested that **21c** is valoneic acid



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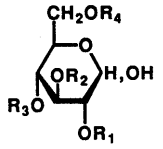
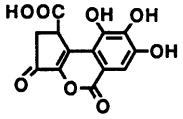


11 : $R_1=R_2=H$, R_3, $R_4=(S)$HHDP
12 : R_1, $R_2=(S)$HHDP, $R_3=R_4=H$
1 : R_1, $R_2=R_3$, $R_4=(S)$HHDP



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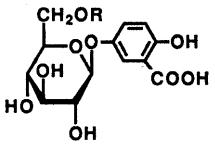
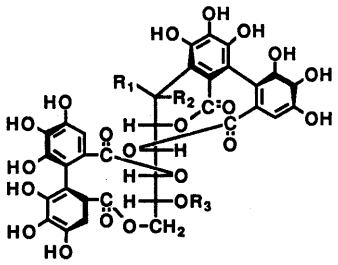
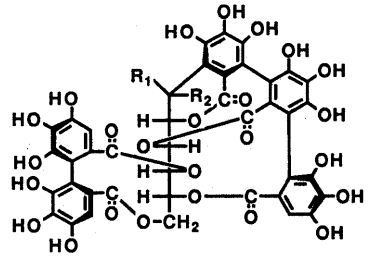


9 : R=H
10 : R=galloyl



14 : R_1=OH, $R_2=R_3=H$
15 : R_1=OH, R_2=H, R_3=galloyl
16 : R_1=H, R_2=OH, R_3=galloyl
17 : $R_1=R_3=H$, R_2=OH



18 : R_1=OH, R_2=H
19 : R_1=H, R_2=OH

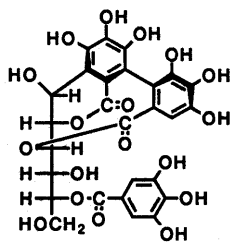


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Chart 3

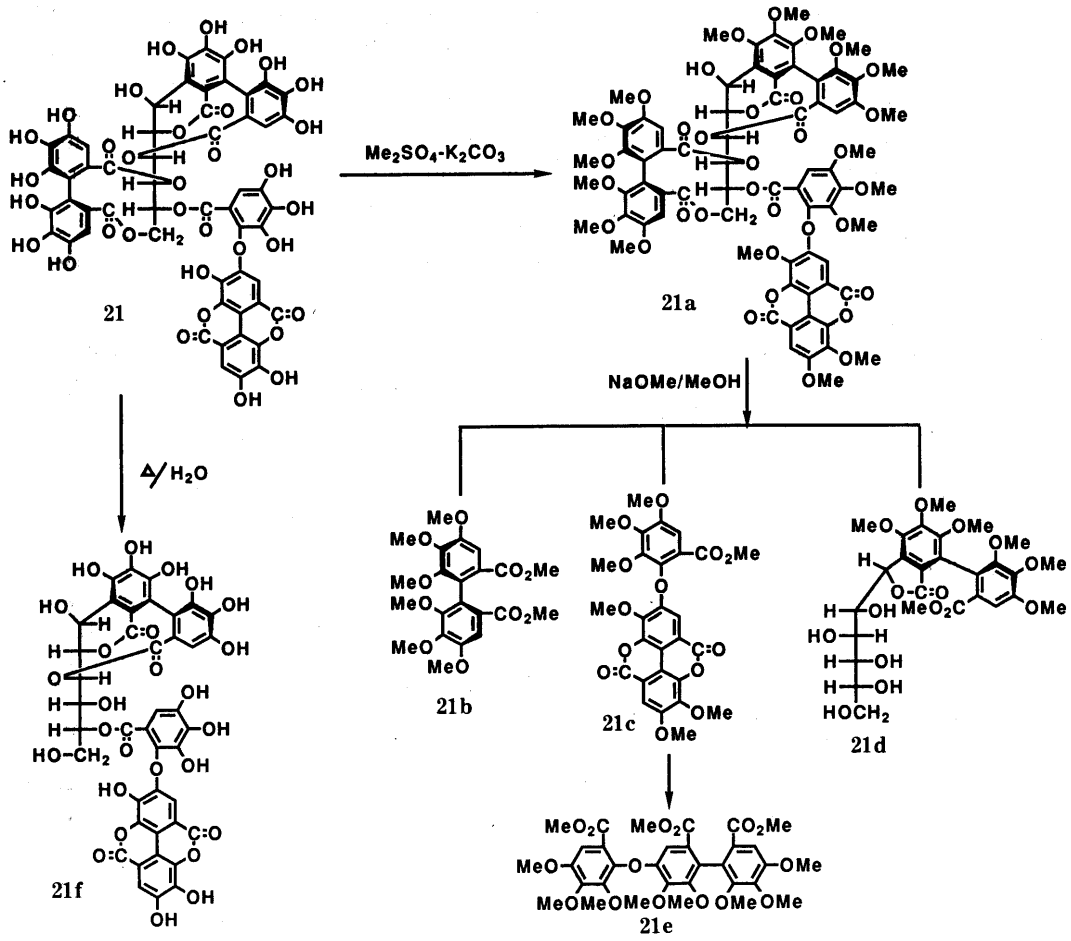


Chart 4

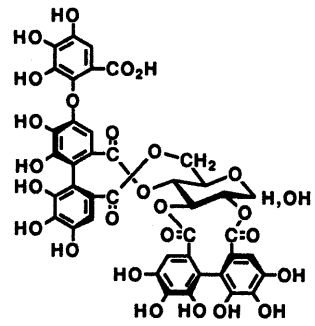
dilactone heptamethylate. The structure of **21c** was further confirmed by alkaline treatment, followed by methylation, yielding racemic trimethyl octa-*O*-methylvaloneate (**21e**).[19] The methanolysate (**21d**) was identical with the product obtained by similar methanolysis of casuarinin pentadecamethyl ether.[15]

To confirm the location of each acyl group, **21** was partially hydrolyzed in hot water to yield ellagic acid and a hydrolysate (**21f**). The ^{1}H-NMR spectrum of **21f** exhibited high-field shifts of the H-4 [δ 3.95 (dd, J=3, 8 Hz)] and H-6 signals (δ 3.80, m), indicating that the location of the HHDP group in **21** is at the C-4 and C-6 positions. On the basis of these findings, the structure of lagerstroemin was established to be as shown by the formula **21**.

The ^{1}H-NMR spectrum of flosin A (**22**) showed complicated signal patterns owing to the presence of α- and β-anomers, but the aliphatic signal patterns resembled those found in pedunculagin (**1**). The aromatic resonances all appearing as a singlet and corresponding to five protons in total suggested the presence of one HHDP and one valoneoyl group. The ^{13}C-NMR chemical shifts (Table II) of sugar carbon signals were in good accord with those of pedunculagin (**1**), suggesting that flosin A has a similar substitution pattern. The negative fast atom bombardment mass spectrum (FAB-MS)[20] exhibited the $[M-H]^-$ peak at m/z 951, which supports the presence of one HHDP and one valoneoyl group. Partial hydrolysis of **22** in hot water to yield 2,3-(*S*)-HHDP-D-glucose (**12**) indicated clearly that the valoneoyl and the HHDP groups are located at the glucose 4,6- and 2,3-positions, respectively. The atropisomerism of the valoneoyl group was determined to be *S* from the result of alkaline methanolysis of the hexadecamethyl ether (**22b**), which yielded trimethyl octa-*O*-methyl-(*S*)-valoneate (**22c**),[19] together with dimethyl (*S*)-hexamethoxydiphenoate (**21b**).

Treatment of **22** with *p*-anisidine in ethanolic acetic acid, followed by sodium cyanoborohydride reduction, yielded the aminoalditol derivative (**22a**). Comparison of the ^{1}H-NMR spectra (Table I) of **22a** and the praecoxin A aminoalditol (**2a**) clearly indicated that there are significant differences in the chemical shifts of the aromatic signals. As mentioned before, since the upfield shift of one of the valoneoyl signals was not observed in **22a**, the valoneoyl group was concluded to be located in the reverse direction. Thus, the structure of flosin A could be represented by the formula **22**.

Reginin A (**23**) was found to be a dimeric hydrolyzable tannin by the observation of the $[M-H]^-$ peak at m/z 1717 in the negative FAB-MS. The ^{1}H-NMR spectrum showed a duplicated signal pattern owing to the presence of α- and β-glucopyranose cores. The aromatic signals all appearing as singlets (see Experimental) corresponded to eight protons in total. The ^{13}C-NMR spectrum (Table II) exhibited eighteen aliphatic signals, among which those at δ 95.3 and 91.8 are typical of the β- and α-anomeric signals, respectively. Treatment of **23** with *p*-anisidine gave the aminoalditol derivative (**23a**), whose ^{1}H-NMR spectrum clearly showed the introduction of one anisidine moiety



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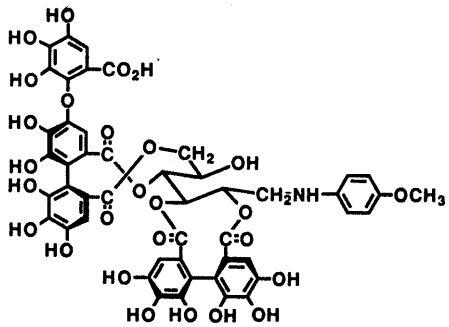
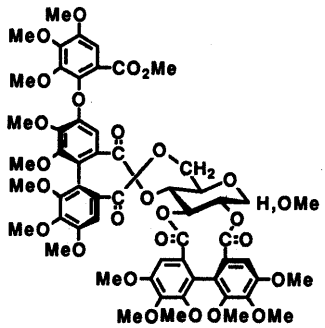
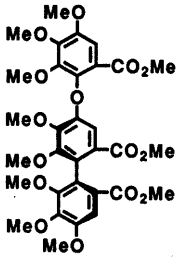


22a

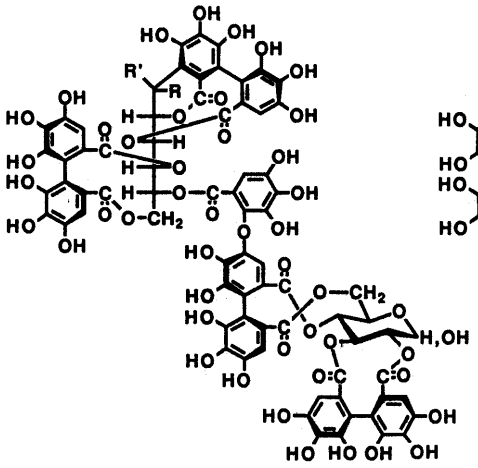


22b

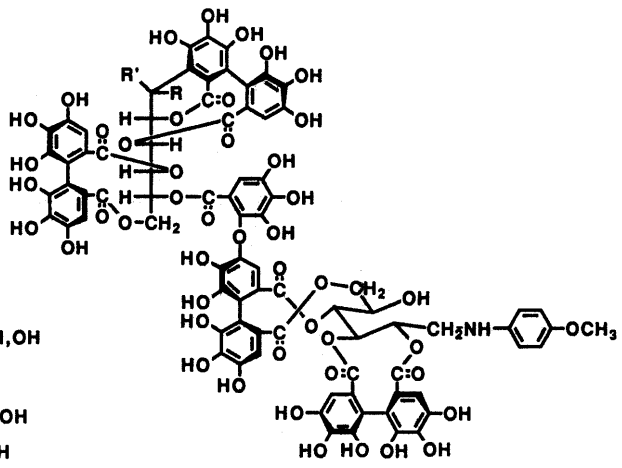


22c

Chart 5



	R	R′
23 :	H	OH
24 :	OH	H



	R	R′
23a :	H	OH
24a :	OH	H

Chart 6

[δ 3.68 (3H, s, OMe) and 6.71 (4H, s)]. The aliphatic signals in the ^{1}H-NMR spectrum of **23a** were unequivocally assigned by ^{1}H–^{1}H shift correlation spectroscopy (COSY), and of these, signals arising from the aminoalditol moiety were closely correlated with those of **22a** and **2a** (Table I). On the other hand, the chemical shifts and the coupling patterns of the remaining aliphatic signals (see Experimental) were comparable to those of casuarinin (**15**). From these findings combined with the observation of eight aromatic one-proton singlets, **23** was considered to be a dimeric hydrolyzable tannin in which the galloyl group in casuarinin (**15**) and the HHDP group in pedunculagin (**1**) are linked through an ether bond, forming a valoneoyl group.

On heating in water, **23** yield 2,3-HHDP-D-glucose (**12**) and lagerstroemin (**21**), while methylation of **23** with dimethyl sulfate and potassium carbonate in dry acetone afforded many products, of which one was found to be identical with the flosin A hexadecamethyl ether (**22b**), thus establishing unambiguously the structure (**23**) of reginin A, including the configuration and the orientation of the valoneoyl group.

Reginin B (**24**) showed, in the negative FAB-MS, the same $[M-H]^-$ peak at m/z 1717 as that of reginin A (**23**). The ^{1}H-NMR spectrum of **24** was also complicated due to the existence of an equilibrium mixture of α- and β-anomers,

TABLE II. ^{13}C-NMR Spectral Data for Reginins A (**23**) and B (**24**), Flosin A (**22**), Pedunculagin (**1**), Casuarinin (**15**) and Stachyurin (**16**)

Glucose		23[a]	24[a]	22[b]	1[b]	15[c]	16[c]
Open-chain form	1′	67.8	64.7			67.8	65.3
	2′	77.5	81.6			77.4	81.8
	3′	70.3	72.3			70.3	72.6
	4′	74.6	73.7			74.6	73.8
	5′	71.5	71.1			71.6	71.5
	6′	65.0	64.4			65.0	65.0
Pyranose form	1 β	95.3	94.9	95.1	95.4		
	α	91.8	91.4	91.6	91.8		
	2 β	78.8	78.2	78.3	78.3		
	α	76.0	75.5	75.6	75.5		
	3 β	77.6	77.2	77.3	77.6		
	α	76.2	75.7	75.6	75.8		
	4 β	70.9	70.9	70.4	69.9		
	α	70.3	70.4	70.1	69.6		
	5 β	72.7	72.2	72.3	72.5		
	α	67.5	67.5	67.3	67.4		
	6 β	64.4	64.0	63.8	63.6		
	α	64.4	64.0	63.8	63.6		

Acetone-d_6 + D_2O, ppm. *a*) Spectra measured at 67.8 MHz. *b*) Spectra measured at 25.05 MHz. *c*) Spectra measured at 100 MHz.

but the ^{13}C-NMR spectrum (Table II) was similar to those of pedunculagin (**1**) plus stachyurin (**16**). Partial hydrolysis of **24** in hot water afforded 2,3-(*S*)-HHDP-D-glucose (**12**) and 5-desgalloyl stachyurin (**17**), and methylation of **24** with dimethyl sulfate and potassium carbonate in acetone, followed by alkaline methanolysis, gave dimethyl (*S*)-hexamethoxydiphenoate (**21b**) and trimethyl octa-*O*-methyl-(*S*)-valoneate (**22c**). From these findings, it was concluded that reginin B has the structure in which the galloyl group in the stachyurin moiety is connected with the 4,6-positioned HHDP group in the pedunculagin moiety through an (*S*)-valoneoyl group. To establish the structure of reginin B including the orientation of the valoneoyl group, the aminoalditol derivative (**24a**) was prepared. The ^{1}H-NMR spectrum (Table I and Experimental) of **24a** clearly showed signals arising from an open-chain form of the *C*-glucoside core and an aminoalditol moiety, and their chemical shifts and coupling patterns agreed well with those of stachyurin (**16**) plus pedunculagin (**1**). In the aromatic field, an upfield shift of H_B in the valoneoyl group, as observed in compounds **2a**, **3a** and **4a**, was not observed, thus confirming that the orientation of the valoneoyl group in reginin B is the same as that in flosin A (**22**) and reginin A (**23**). Accordingly, the structure of reginin B is represented by the formula **24**.

In conclusion, the preparation of the aminoalditol derivatives of hydrolyzable tannins which lack an acyl group at the glucose C-1 position was proved to be a useful tool for determining their structures. In particular, by using this method, the orientation of the valoneoyl group located at the glucose C-4 and C-6 positions was found to be readily determinable by observing the ^{1}H-NMR chemical shift of the H_B signal.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter (cell length: 0.5 dm). EI-MS were measured with a JEOL D-300 spectrometer, while field desorption mass spectrum (FD-MS) and FAB-MS were taken with a JEOL DX-300 instrument. ^{1}H (100 MHz)- and ^{13}C (25.05 MHz)-NMR spectra were recorded on JEOL PS-100 and JEOL FX-100 spectrometers, respectively, and ^{1}H (270 MHz)- and ^{13}C (67.8 MHz)-NMR spectra on a JEOL GX-270 spectrometer, with tetramethylsilane (TMS) as an internal standard, the chemical shifts being given in δ (ppm). Column chromatography was carried out with Sephadex LH-20 (25—100 μ, Pharmacia Fine Chemical Co., Ltd.), MCI-gel CHP 20P (75—150 μ, Mitsubishi Chemical Industries Co., Ltd.), TSK gel Toyopearl HW-40F (30—60 μ, Toso Co., Ltd.), TSK gel Phenyl Toyopearl 650 M (88 μ, Toso Co., Ltd.), Cosmosil 75 C_{18}-OPN (42—105 μ, Nacalai Tesque Inc.), Bondapak C_{18}/Porasil B (37—75 μ, Waters Associates Inc.) and Kieselgel 60 (70—230 mesh, Merck). Thin-layer chromatography (TLC) was conducted on precoated Silica gel 60 F_{254} plates (Merck, 0.20 mm thick) and precoated cellulose F_{254} plates (Merck, 0.10 mm thick). Spots were visualized under ultra violet light and by spraying $FeCl_3$ solution (for phenolics), $NaNO_2$–HOAc solution (for ellagitannins) or 10% sulfuric acid, followed by heating (for phenolics and methylates).

General Procedures for Preparing the Aminoalditol Derivatives (1a—7a) A mixture of a hydrolyzable tannin (**1**—**7**) (10—100 mg) and *p*-anisidine (2—20 mg) in 20% ethanolic acetic acid (1—5 ml) was stirred at room temperature for 2 h, and the mixture was treated with sodium cyanoborohydride (5—20 mg) at room temperature for 1 h. After addition of 1 N HCl, the product was purified by Sephadex LH-20 chromatography with EtOH–H_2O to give the corresponding aminoalditol derivative (**1a**—**7a**) in 50—80% yield.

Pedunculagin Aminoalditol (1a) An off-white amorphous powder, $[\alpha]_D^{13}$ +108.7° (*c* = 0.96, MeOH). *Anal.* Calcd for $C_{41}H_{33}NO_{22}\cdot 6H_2O$: C, 49.29; H, 4.54; N, 1.39. Found: C, 49.33; H, 4.34; N, 1.39. Negative FAB-MS *m/z*: 890 $[M-H]^-$. ^{1}H-NMR: see Table I.

Praecoxin A Aminoalditol (2a) An off-white amorphous powder, $[\alpha]_D^{30}$ +77.9° (*c* = 1.8, MeOH). *Anal.* Calcd for $C_{48}H_{35}NO_{27}$: C, 53.58; H, 3.50; N, 1.32. Found: C, 53.56; H, 3.54; N, 1.33. ^{1}H-NMR: see Table I.

Rugosin B Aminoalditol (3a) An off-white amorphous powder, $[\alpha]_D^{24}$ +53.8° (*c* = 0.9, MeOH), *Anal.* Calcd for $C_{48}H_{37}NO_{27}$: C, 54.39; H, 3.49; N, 1.32. Found: C, 54.20; H, 3.57; N, 1.35. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz): 7.13 (2H, s, galloyl H), 7.12 (2H, s, galloyl H). For other signals, see Table I.

Camelliin A Aminoalditol (4a) An off-white amorphous powder, $[\alpha]_D^{20}$ +96.5° (*c* = 1.0, MeOH). *Anal.* Calcd for $C_{82}H_{66}N_2O_{44}\cdot 2H_2O$: C, 54.17; H, 3.88; N, 1.54. Found: C, 53.81; H, 3.68; N, 1.40. Negative FAB-MS *m/z*: 1781 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 7.00 (2H, s, galloyl H), 6.87, 6.65, 6.63, 6.56 (each 1H, s, arom. H), 5.66 (1H, dd, *J* = 9, 2 Hz, H-3′), 5.38—5.45 (1H, m, H-2′), 5.11—5.21 (1H, m, H-4′), 4.35 (1H, dd, *J* = 12, 3 Hz, H-6′), 3.95 (1H, d, *J* = 9 Hz, H-5′), 4.50—3.60 (1H, m, H-1′), 2.99 (1H, dd, *J* = 14, 10 Hz, H-1′). For other signals, see Table I.

1-Desgalloyleugeniin Aminoalditol (5a) An off-white amorphous powder, $[\alpha]_D^{20}$ +78.9° (*c* = 0.8, MeOH). *Anal.* Calcd for $C_{41}H_{35}NO_{22}\cdot H_2O$: C, 51.02; H, 4.49; N, 1.45. Found: C, 51.04; H, 4.49; N, 1.45. Negative FAB-MS *m/z*: 892 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz): 7.17 (2H, s, galloyl H), 7.22 (2H, s, galloyl H). For other signals, see Table I.

Gemin D Aminoalditol (6a) An off-white amorphous powder, $[\alpha]_D^{20}$ +80.7° (*c* = 2.0, MeOH). *Anal.* Calcd for $C_{34}H_{31}NO_{18}$: C, 55.06; H, 4.18; N, 1.89. Found: C, 54.83; H, 4.31; N, 1.77. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz): 7.17 (2H, s, galloyl H). For other signals, see Table I.

Rugosin E Aminoalditol (7a) An off-white amorphous powder, $[\alpha]_D^{21}$ +85.8° (*c* = 1.0, acetone). *Anal.* Calcd for $C_{82}H_{63}NO_{48}\cdot H_2O$: C, 53.28; H, 3.52; N, 0.75. Found: C, 53.12; H, 3.65; N, 0.81. Negative FAB-MS *m/z*: 1828 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 7.21, 7.17, 7.01, 6.97 (each 2H, s, galloyl H), 6.67, 6.46 (each 1H, s, arom. H), 6.09 (1H, d, *J* = 8 Hz, H-1′), 5.80 (1H, t, *J* = 10 Hz, H-3′), 5.53 (1H, dd, *J* = 4, 10 Hz, H-2′), 5.33 (1H, dd, *J* = 5, 12 Hz, H-6′), 5.16 (1H, t, *J* = 10 Hz, H-4′), 4.47 (1H, dd, *J* = 5, 10 Hz, H-5′), 3.78 (1H, d, *J* = 12 Hz, H-6′). For other signals, see Table I.

Isolation of Tannins Dried leaves of *L. flos-reginae*, collected in Java, Indonesia, in May, were extracted five times with 70% aqueous actone at room temperature. The extract was concentrated under reduced pressure, and the brown precipitates formed were filtered off with the aid of Celite 545. The filtrate was partitioned with ethyl acetate, and the aqueous layer was applied to a Sephadex LH-20 column, eluting with H_2O containing increasing proportions of MeOH to afford two fractions. Fraction 1 was repeatedly chromatographed over Sephadex LH-20 with EtOH–H_2O and MCI-gel CHP 20P with H_2O–MeOH to give 3-*O*-caffeoylquinic acid (**8**) (10 mg), gentisic acid 5-*O*-β-D-glucopyranoside (**9**) (132 mg), brevifolin carboxylic acid (**13**) (70 mg) and 4,6-(*S*)-HHDP-D-glucose (**11**) (110 mg). Fraction 2 was subjected to MCI-gel CHP 20P chromatography with

H_2O–MeOH to afford three fractions, 2-a, 2-b and 2-c. Fraction 2-a was repeatedly chromatographed over MCI-gel CHP 20P, Sephadex LH-20 and TSK gel Phenyl Toyopearl 650 M with H_2O–MeOH to give 2,3-(*S*)-HHDP-D-glucose (**12**) (70 mg), punicacortein A (**20**) (50 mg), 5-desgalloylstachyurin (**17**) (52 mg) and vascalagin (**19**) (80 mg). Fraction 2-b was repeatedly chromatographed over Sephadex LH-20 (H_2O–MeOH–50% acetone), TSK gel Toyopearl HW-40F (H_2O–MeOH–50% acetone), TSK gel Phenyl Toyopearl 650 M (H_2O–MeOH) and Cosmosil 75 C_{18}-OPN (H_2O–MeOH) to give reginins A (**23**) (500 mg) and B (**24**) (650 mg), flosin A (**22**) (98 mg), casuariin (**14**) (230 mg), stachyurin (**16**) (158 mg), castalagin (**18**) (170 mg) and pedunculagin (**1**) (1.35 g). Fraction 2-c was repeatedly chromatographed over Sephadex LH-20 (H_2O–MeOH–50% acetone), TSK gel Toyopearl HW-40F (MeOH, 50% acetone), TSK gel Phenyl Toyopearl 650 M (H_2O–MeOH) and Cosmosil 75 C_{18}-OPN (H_2O–MeOH) to give gentisic acid 5-*O*-β-D-(6′-*O*-galloyl)-glucopyranoside (**10**) (10 mg), casuarinin (**15**) (3.0 g) and lagerstroemin (**21**) (50 mg). Compounds **8**—**20** were identified by direct comparisons of their physical and spectral data with those of authentic samples.

Lagerstroemin (21) Colorless needles (H_2O), mp 230 °C (dec.), $[\alpha]_D^{20}$ +7.3° (*c* = 1.0, acetone), *Anal.* Calcd for $C_{55}H_{32}O_{34}\cdot 7H_2O$: C, 48.46; H, 3.55. Found: C, 47.98; H, 3.14. Negative FAB-MS *m/z*: 1235 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 7.64, 7.20, 7.18 (each 1H, s valoneoyl H), 6.83, 6.59, 6.41 (each 1H, s, arom. H), 5.62 (1H, d, *J* = 5 Hz, H-1), 5.44 (1H, br s, H-3), 5.42 (1H, dd, *J* = 2, 9 Hz, H-4), 5.24 (1H, dd, *J* = 3, 9 Hz, H-5), 4.69 (1H, dd, *J* = 3, 13 Hz, H-6), 4.65 (1H, dd, *J* = 2, 5 Hz, H-2), 3.37 (1H, d, *J* = 13 Hz, H-6). ^{13}C-NMR (acetone-d_6, 67.8 MHz): 169.7, 169.3, 168.9, 165.6, 163.8 (–COO–), 160.7, 160.6 (δ-lactone), 149.9, 149.2, 145.9, 145.8, 145.3, 144.6, 144.5, 143.5, 141.6, 140.9, 140.4, 140.2, 139.0, 137.4, 137.3, 137.1, 137.0, 136.0, 135.0, 127.1, 126.6, 124.6, 119.8, 117.6, 116.4, 116.2, 116.1, 115.4, 115.1, 113.9, 113.1, 111.7, 109.8, 109.6, 108.7, 108.6, 108.4, 107.2, 105.5 (arom. C), 76.9 (C-2), 73.9 (C-4), 70.6 (C-5), 69.6 (C-3), 66.8 (C-1), 64.5 (C-6).

Methylation of 21 A mixture of **21** (200 mg), dimethyl sulfate (2 ml) and anhydrous potassium carbonate (2 g) in dry acetone (30 ml) was refluxed for 4 h. After removal of the inorganic salts by filtration, the filtrate was concentrated to a syrup and subjected to silica gel column chromatography [benzene–acetone (8 : 1)] to afford the octadecamethylate (**21a**) (94 mg), colorless needles (MeOH), mp 203—205 °C, $[\alpha]_D^{23}$ −35.2° (*c* = 0.6, acetone), *Anal.* Calcd for $C_{73}H_{68}O_{34}\cdot 1/2H_2O$: C, 58.51; H, 4.64. Found: C, 58.11; H, 4.64. FD-MS *m/z*: 1488 $[M^+]$. ^{1}H-NMR ($CDCl_3$, 270 MHz), 7.70, 7.31, 7.29, 7.04, 6.79, 6.50 (each 1H, s, arom. H), 5.52 (1H, dd, *J* = 2, 5 Hz, H-4), 5.42 (1H, d, *J* = 5 Hz, H-1), 5.33 (1H, t, *J* = 2 Hz, H-2), 4.79 (1H, dd, *J* = 3, 13 Hz, H-6), 4.27, 4.16, 4.04, 4.01, 4.00, 3.99, 3.98, 3.97, 3.96, 3.95, 3.93 (×2), 3.86, 3.84, 3.77, 3.71, 3.64, 3.44 (each 3H, s, OMe).

Alkaline Methanolysis of 21a **21a** (80 mg) was methanolyzed with 1% sodium methoxide in methanol (3 ml) at room temperature overnight. The reaction mixture was neutralized with Amberlite IR 120B (H^+ form), concentrated *in vacuo* and separated by silica gel chromatography. Elution with benzene–acetone (43 : 2) yielded dimethyl (*S*)-hexamethoxydiphenoate (**21b**) (12 mg) and valoneic acid dilactone heptamethylate (**21c**) (13 mg), colorless needles (MeOH), mp 264—265 °C, *Anal.* Calcd for $C_{28}H_{24}O_{13}$: C, 59.16; H, 4.26. Found: C, 59.28; H, 4.27. EI-MS *m/z*: 568 $[M]^+$. ^{1}H-NMR ($CDCl_3$, 100 MHz): 7.72, 7.35, 7.27 (each 1H, s, arom. H), 4.36, 4.20, 4.04, 3.99, 3.97, 3.80, 3.75 (each 3H, s, OMe). Further elution with benzene–EtOH (10 : 1) afforded the hydrolysate (**21d**) (10 mg), a white amorphous powder, $[\alpha]_D^{20}$ −40.4° (*c* = 0.6, acetone), FD-MS *m/z*: 598 $[M]^+$. ^{1}H-NMR (acetone-d_6, 270 MHz): 7.42 (1H, s, arom. H), 5.73 (1H, d, *J* = 2 Hz, H-1), 4.47 (1H, br d, *J* = 7 Hz, H-2), 4.15 (1H, d, *J* = 8 Hz, H-4), 4.05, 3.98, 3.95, 3.89, 3.59, 3.56 (×2) (each 3H, s, OMe).

Alkaline Treatment of 21c, Followed by Methylation A solution of **21c** (10 mg) in 5% NaOH [H_2O–MeOH (1 : 1)] (2 ml) was heated at 70 °C for 30 min. The reaction mixture was treated with dimethyl sulfate (1 ml) at 70 °C for 30 min. The solution was acidified with 1 N HCl (5 ml) and extracted three times with ether. The organic layer was dried over sodium sulfate, concentrated to dryness and treated with ethereal diazomethane. After evaporation of the solvent, the syrupy residue was chromatographed over silica gel with benzene–acetone (19 : 1) to give trimethyl octa-*O*-methyl valoneate (**21e**) (5 mg).

Partial Hydrolysis of 21 **21** (100 mg) in water was heated at 80 °C for 3 h. After filtration of the resulting precipitates (ellagic acid), the filtrate was directly subjected to Sephadex LH-20 chromatography with 60% MeOH to give the partial hydrolysate (**21f**) (23 mg), a tan amorphous powder, $[\alpha]_D^{20}$ −45.6° (*c* = 0.6, MeOH), Negative FAB-MS *m/z*: 933 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 7.65, 7.19, 7.15, 6.21 (each 1H, s, arom. H), 5.55 (1H, d, *J* = 5 Hz, H-1), 5.23 (1H, dd, *J* = 2, 3 Hz, H-3), 4.98 (1H, dd, *J* = 3, 8 Hz, H-5), 4.78 (1H, dd, *J* = 2, 5 Hz, H-2), 3.95 (1H, dd, *J* = 3, 8 Hz, H-4), 3.80 (2H, m, H-6).

Flosin A (22) An off-white amorphous powder, $[\alpha]_D^{26}$ +32° (*c* = 1.1, MeOH), *Anal.* Calcd for $C_{41}H_{28}O_{27}$: C, 51.69; H, 2.96. Found: C, 51.82; H, 2.88. Negative FAB-MS *m/z*: 951 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz): 7.07, 7.06 (1H in total, each s, valoneoyl H), 6.66, 6.65 (1H in total, each s, arom. H), 6.58 (1H, s, arom. H), 6.34, 6.26 (1H, in total, each s, arom. H), 6.30, 6.29 (1H in total, each s, arom. H), 3.50—5.50 (7H, m, glc. H). ^{13}C-NMR (acetone-d_6 + D_2O, 25.05 MHz): 169.3, 169.0, 168.8, 168.5, 168.1, 167.2 (–COO–). For other signals, see Table II.

Partial Hydrolysis of 22 A solution of **22** (10 mg) in water (2 ml) was heated on a water bath (90 °C) for 15 h. The reaction mixture was subjected to MCI-gel CHP 20P chromatography with 10% MeOH to yield 2,3-(*S*)-HHDP-D-glucose (**12**) (2 mg).

Methylation of 22 A mixture of **22** (20 mg), dimethyl sulfate (0.5 ml) and anhydrous potassium carbonate (1 g) in dry acetone (5 ml) was heated under reflux for 5 h. Work-up as described above afforded the hexadecamethylates as an inseparable mixture (**22b**) (11 mg), a white amorphous powder, FD-MS *m/z*: 1176 $[M]^+$. ^{1}H-NMR ($CDCl_3$, 270 MHz): 7.25, 7.21 (valoneoyl H_c), 6.78, 6.73, 6.72, 6.56 (valoneoyl H_a and HHDP-H), 6.47, 6.43 (valoneoyl H_b), 5.04 (t, *J* = 10 Hz, α, β-H-3), 4.96—5.19 (α, β-H-2, α, β-H-4, α, β-H-6), 4.91 (d, *J* = 5 Hz, α-H-1), 4.58 (d, *J* = 8 Hz, β-H-1), 4.23, 4.21 (each d, *J* = 9 Hz, α, β-H-5), 3.55—4.10 (OMe and α, β-H-6).

Alkaline Methanolysis of 22b **22b** (10 mg) was treated with 2% sodium methoxide in dry methanol (0.5 ml) at room temperature for 24 h. After neutralization with Amberlite IR 120B (H^+ form), the solution was concentrated *in vacuo* and the residue was chromatographed over silica gel with benzene–acetone (8 : 1) to furnish dimethyl (*S*)-hexamethoxydiphenoate (**21b**) (4 mg) and trimethyl octa-*O*-methyl-(*S*)-valoneate (**22c**) (3 mg).

Preparation of the Aminoalditol Derivative (22a) **22** (10 mg) was treated as described in the general procedure to furnish the aminoalditol (**22a**) as a brown amorphous powder, $[\alpha]_D^{30}$ +114.5° (*c* = 0.5, MeOH), *Anal.* Calcd for $C_{48}H_{35}NO_{27}$: C, 53.58; H, 3.50; N, 1.32. Found: C, 53.31; H, 3.57; N, 1.42. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 6.70, 6.53 (each 1H, s, HHDP-H). For other signals, see Table I.

Reginin A (23) An off-white amorphous powder, $[\alpha]_D^{26}$ +62° (*c* = 0.9, MeOH), *Anal.* Calcd for $C_{75}H_{50}O_{48}$: C, 52.39; H, 2.91. Found: C, 52.20; H, 2.51. Negative FAB-MS *m/z*: 1717 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 100 MHz): 7.03, 7.02 (1H in total, each s, valoneoyl H_c), 6.82, 6.81 (1H in total, each s, arom. H), 6.65, 6.64 (1H in total, each s, arom. H), 6.58 (1H, s, arom. H), 6.58 (1H, s, arom. H), 6.56. 6.52 (1H in total, each s, arom. H), 6.31 (1H, s, arom. H), 6.35, 6.27 (1H in total, each s, arom. H), 5.60 (1H, d, *J* = 5 Hz, H-1′), 3.50—5.47 (13 H, m, glc. H). ^{13}C-NMR (acetone-d_6 + D_2O, 67.8 MHz): see Table II.

Methylation of 23 A mixture of **23** (50 mg), dimethyl sulfate (2 ml) and anhydrous potassium carbonate (2 g) in dry acetone (10 ml) was heated under reflux for 5 h. The reaction mixture was chromatographed over silica gel with benzene–acetone to afford among many uncharacterized products, a product (**3a**) (4 mg).

Partial Hydrolysis of 23 An aqueous solution (3 ml) of **23** (50 mg) was heated at 80—90 °C for 20 h. The reaction mixture was directly subjected to MCI-gel CHP 20P chromatography with H_2O–MeOH to afford lagerstroemin (**21**) (910 mg) and 2,3-(*S*)-HHDP-D-glucose (**12**) (5 mg).

Preparation of the Aminoalditol Derivative (23a) **23** (15 mg) was treated as described in the general procedure to give the aminoalditol (**23a**) (13 mg) as a brown amorphous powder, $[\alpha]_D^{30}$ +34.2° (*c* = 0.8, MeOH), *Anal.* Calcd for $C_{82}H_{57}NO_{48}\cdot H_2O$: C, 52.93; H, 3.28; N, 0.75. Found: C, 52.77; H, 3.50; N, 1.00. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 6.88, 6.65, 6.62, 6.59, 6.58 (each 1H, s, arom. H), 5.61 (1H, d, *J* = 5 Hz, H-1′), 5.48 (1H, t, *J* = 2 Hz, H-3′), 5.40 (1H, dd, *J* = 2, 8 Hz, H-4′), 5.35 (1H, dd, *J* = 3, 8 Hz, H-5′), 4.82 (1H, dd, *J* = 3, 14 Hz, H-6′), 4.63 (1H, dd, *J* = 2, 5 Hz, H-2′), 3.86 (1H, d, *J* = 14 Hz, H-6′). For other signals, see Table I. ^{13}C-NMR (acetone-d_6 + D_2O, 25.05 MHz): 169.9, 169.8, 169.5 (×3), 169.1, 168.7 (×3) (–COO–), 165.2, 153.1 (anisidine moiety), 77.0 (C-2′), 76.2 (C-3), 74.2 (C-4), 73.8 (C-4′), 73.0 (C-2), 71.3 (C-5′), 70.1 (C-3′), 68.7 (C-5), 67.1 (C-1′), 65.0 (C-6′), 61.7 (C-6), 44.7 (C-1).

Reginin B (24) An off-white amorphous powder, $[\alpha]_D^{26}$ +26° (*c* = 1.3, MeOH), *Anal.* Calcd for $C_{75}H_{50}O_{48}\cdot 3H_2O$: C, 50.79; H, 3.27. Found: C, 50.87; H, 3.06. Negative FAB-MS *m/z*: 1717 $[M-H]^-$. ^{1}H-NMR (acetone-d_6 + D_2O, 270 MHz): 7.04, 7.03 (1H in total, s, valoneoyl H_c), 6.95, 6.94 (1H in total, s, arom. H), 6.65, 6.64 (1H in total, arom. H),

6.62, 6.61 (1H in total, s, arom. H), 6.60 (1H, s, arom. H), 6.55, 6.54 (1H, in total, s, arom. H), 6.31, 6.30 (1H in total, s, arom. H), 6.30, 6.25 (1H in total s, arom. H), 3.50—5.70 (14H, glc. H). ^{13}C-NMR (acetone-d_6+D_2O, 67.8 MHz): see Table II.

Methylation of 24, Followed by Alkaline Methanolysis A mixture of **24** (100 mg), dimethyl sulfate (2 ml) and anhydrous potassium carbonate (2 g) in dry acetone (20 ml) was heated under reflux for 7 h. The reaction mixture was worked up as before to afford a mixture of methylates (60 mg). A part (20 mg) of this methylate was treated with 2% sodium methoxide in dry MeOH (1 ml) at room temperature for 24 h. Separation of the reaction products as described for **22b** gave dimethyl (*S*)-hexamethoxydiphenoate (**21b**) (5 mg) and trimethyl octa-*O*-methyl-(*S*)-valoneate (**22c**) (3 mg).

Partial Hydrolysis of 24 A solution of **24** (50 mg) in water (5 ml) was heated at 80—90 °C for 20 h. The reaction products were separated by MCI-gel CHP 20P chromatography with H_2O–MeOH to afford 5-desgalloyl stachyurin (**17**) (5 mg) and 2,3-(*S*)-HHDP-D-glucose (**12**) (2 mg).

Preparation of the Aminoalditol Derivative (24a) **24** (50 mg) was treated as described in the general procedure to give **24a** (28 mg), a brown amorphous powder, $[\alpha]_D^{30}$ +73° (*c*=0.8, MeOH), *Anal.* Calcd for $C_{82}H_{57}NO_{48}$: C, 52.93; H, 3.28; N, 0.75. Found: C, 52.97; H, 3.28; N, 0.87. ^{1}H-NMR (acetone-d_6+D_2O, 270 MHz): 6.98, 6.60, 6.59, 6.58, 6.56, 6.54, 6.50 (each 1H, s, arom. H), 5.70 (1H, dd, *J*=2, 8 Hz, H-4′), 5.36 (1H, dd, *J*=3, 8 Hz, H-5′), 5.34 (1H, t, *J*=2 Hz, H-3′), 4.98 (1H, d, *J*=2 Hz, H-1′), 4.87 (1H, dd, *J*=3, 13 Hz, H-6′), 4.83 (1H, t, *J*=2 Hz, H-2′), 3.91 (1H, d, *J*=13 Hz, H-6′). For other signals, see Table I.

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