Three Novel *C*-Glycosidic Ellagitannins, Rhoipteleanins H, I, and J, from *Rhoiptelea chiliantha*

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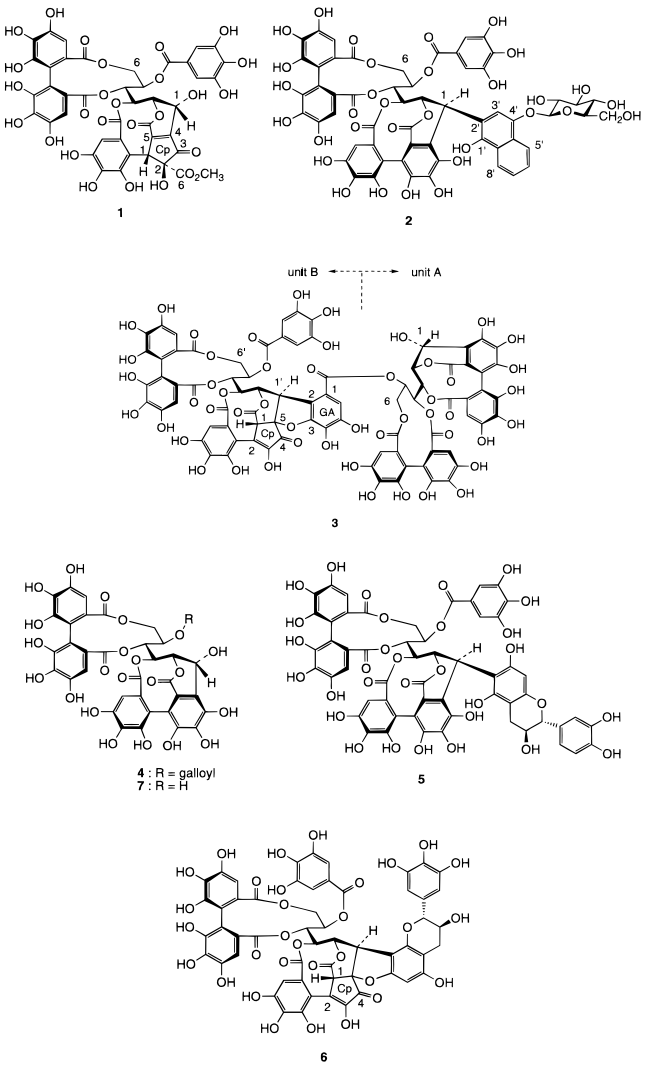
Three novel *C*-glycosidic ellagitannins named rhoipteleanins H (**1**), I (**2**), and J (**3**) were isolated from the fruits and bark of *Rhoiptelea chiliantha* Diels et Hand.-Mazz. (Rhoipteleaceae), and the structures were elucidated on the basis of detailed spectroscopic analysis and chemical evidence. Rhoipteleanin H possesses a unique cyclopentenone carboxyl moiety, which is probably formed by oxidation and subsequent rearrangement of an aromatic ring of a usual *C*-glycosidic ellagitannin. Rhoipteleanin I is the first ellagitannin having a hydroxynaphthalene glucoside moiety. Rhoipteleanin J is a dimeric ellagitannin generated by dehydrative coupling between two molecules of a monomeric *C*-glycosidic ellagitannin and subsequent oxidation of an aromatic ring. From a chemotaxonomic viewpoint, presence of these characteristic ellagitannins in this plant provides a further support for the establishment of the order Rhoipteleales comprising Rhoipteleaceae as the only family.

Rhoiptelea chiliantha Diels et Hand.-Mazz., a tree distributed in southern China and northern Vietnam, is the only species of the family Rhoipteleaceae. The systematic position of this monotypic family is still unclear, and several opinions have so far been published on the basis of morphological, anatomical, and palynological evidence.[1] Our chemical research of this plant revealed the presence of some characteristic secondary metabolites, that is, triterpene−lignan esters,[2] a rearranged ursane triterpene,[3] a lupane triterpene and two triterpene caffeates,[4] dimeric ellagitannins,[5,6] diarylheptanoids,[7] and euphane-type triterpene tridesmosides.[8] The presence of these characteristic metabolites chemotaxonomically supported the establishment of the order Rhoipteleales.[7,9] The dimeric ellagitannins, isolated from the fruits as the major phenolic constituents and named rhoipteleanins A−F,[5,6] have unique structures that were biogenetically formed by intermolecular oxidative C−C coupling of two molecules of monomers. Numerous dimeric ellagitannins known before, except for the *C*-glycosidic type, had been believed to be exclusively biosynthesized by intermolecular C−O oxidative coupling of pyrogallol rings;[10] therefore, the isolation of the rhoipteleanins A−F suggested that the metabolism of hydrolyzable tannins in this plant is unusual. Further investigation of the minor polyphenolic metabolites of this plant led to the isolation of three novel *C*-glycosidic ellagitannins named rhoipteleanins H (**1**), from the fruits, and I (**2**) and J (**3**), from the bark. This paper deals with the isolation and structure elucidation of these compounds.

Results and Discussion

The MeOH extract of dried fruits was suspended in H_2O and extracted with ethyl ether and ethyl acetate, successively. The H_2O layer was separated by a combination of column chromatographies over MCI-gel CHP 20P, Sephadex LH-20, and Bondapak ODS to afford rhoipteleanin H (**1**) (0.004% based on the dry w) together with rhoipteleanins A−G.[5,6] The EtOH extract of the air-dried bark was separated in a similar manner to afford rhoipteleanins I (**2**)(0.006%) and J (**3**) (0.0007%), together with seven known tannins: casuarinin (**4**);[11,12] 1-*O*-galloyl-2,3;4,6-bis-(*S*)-4,4′,5,5′,6,6′-hexahydroxydiphenoyl(HHDP)-*β*-D-glucose;[11] 1,2,3,4,6-penta-*O*-galloyl-*β*-D-glucose;[13] casuariin (**7**);[11,12] pterocarinin A;[14] 2,3,4,6-*bis*-(*S*)-HHDP-D-glucose;[15] and alienanin B.[16]



Rhoipteleanin H (**1**) was characterized as an ellagitannin on the basis of its dark blue coloration with $FeCl_3$ reagent

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Table 1. ^{1}H NMR Data for Glucose and Cyclopentenone Moieties of Compounds **1**−**6** [in $(CD_3)_2CO + D_2O$]

		2		**3**				
glucose	**1**	open chain	glycoside unit	unit A	unit B	**4**	**5**	**6**
1	5.42 (dd 3, 6)	5.04 (d 2)	4.69 (d, 8)	5.63 (d 5)	4.15 (s)	5.64 (d 5)	4.68 (s)	4.09 (s)
2	4.98 (d 6)	5.17 (t 2)	3.56 (dd, 8, 9)	4.64 (dd 2, 5)	4.61 (s)	4.70 (dd 2, 5)	4.79 (br s)	5.37 (s)
3	6.10 (d 2)	5.34 (t 2)	3.45 (t, 9)	5.76 (br. s)	5.48 (d 8)	5.48 (t 2)	5.21 (t 2)	5.19 (d 6)
4	5.59 (dd 2, 10)	5.81 (dd 2, 9)	3.41 (t, 9)	5.57 (t 4)	5.51 (t 8)	5.50 (dd 2, 9)	5.78 (dd 2, 8)	5.79 (dd 6, 8)
5	5.38 (dd 4, 10)	5.41 (dd 3, 9)	3.16 (ddd, 2, 5, 9)	5.91 (br s)	5.68 (br d 8)	5.37 (dd 3, 9)	5.60 (dd 3, 8)	5.63 (d 7)
6	5.01 (dd 4, 13)	4.91 (dd 3, 14)	3.82 (dd, 2, 13)	4.70 (br d 12)	4.70 (br d 12)	4.90 (dd 3, 12)	4.95 (dd 3, 12)	4.59 (dd 3, 12)
	4.02 (d 13)	4.09 (d 14)	3.66 (dd, 5, 13)	4.26 (dd 2, 12)	3.62 (dd 3, 12)	4.11 (d 13)	4.07(d 12)	4.16 (d 12)
cyclopen-tenone								
1	5.32 (d, 3)				4.48 (s)			4.36 (s)
OCH_3	3.76 (3H, s)							

Table 2. ^{13}C NMR Data for Glucose and Cyclopentenone Moieties of Compounds **1**−**6** [in $(CD_3)_2CO + D_2O$]

		2		**3**				
glucose	**1**	open-chain	pyranoside	unit A	unit B	**4**	**5**	**6**
1	62.8	40.4	103.2	68.3	47.5	67.8	38.3	46.2
2	79.3	79.5	74.1	77.4	83.6	77.4	81.2	81.1
3	67.0	74.4	77.3	72.7	78.0	70.3	74.9	76.4
4	73.4	73.2	70.7	75.2	71.6	74.6	73.3	70.1
5	69.7	71.1	77.4	73.0	71.6	71.6	71.3	72.0
6	64.7	64.4	62.4	63.6	65.9	65.0	64.5	64.5
cyclopen-tenone								
1	44.9				48.3			49.6
2	82.7				137.2			139.4
3	200.4				149.8			149.3
4	142.7				195.3			195.7
5	155.5				91.6			90.7
6	171.5							
OCH_3	53.8							

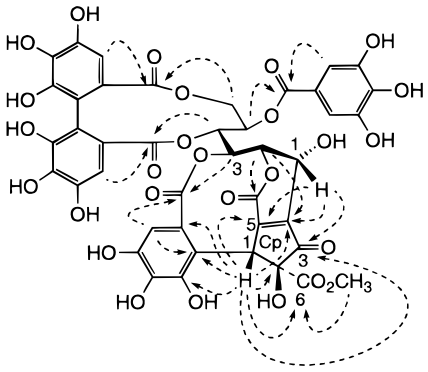


Figure 1. Selected HMBC correlations (H→C) observed for **1**.

and reddish brown coloration with $NaNO_2$−AcOH reagent.[17] The ^{1}H NMR spectrum exhibited a two-proton aromatic singlet signal (δ 7.20) due to a galloyl group, three one-proton aromatic singlets (δ 6.91, 6.60, and 6.43), and aliphatic proton signals attributable to six methines, a methylene, and a methoxyl group (Table 1). The similarity of the chemical shifts and coupling pattern of the five aliphatic methine and methylene protons to those of casuarinin (**4**),[11,12] suggested the presence of an open-chain glucose. The ^{13}C NMR spectrum showed five conjugated ester carboxyl signals [δ 169.1, 168.8 (×2), 166.8, and 163.2] and signals arising from four pyrogallol rings, one of which is attributable to the galloyl group. The HMBC spectrum showed correlations of these ester carbons with the glucose and aromatic protons, confirming the connectivity of ester linkages, including the location of the galloyl group at glucose C-5, as shown in Figure 1. The correlations also revealed the presence of an HHDP group attached to C-4 and C-6 positions of the open-chain glucose moiety. The remaining carbon signals indicated the presence of a tetrasubstituted double bond (cyclopentenone: Cp-4 and -5), a conjugated ketone (Cp-3), a benzyl methine (Cp-1), an oxygen-bearing quaternary carbon (Cp-2), a nonconjugated ester carbonyl (Cp-6), and a methoxyl group (Table 2). In the HSQC spectrum, the benzyl methine carbon (Cp-1) was correlated with a proton signal at δ 5.32, and the ^{1}H−^{1}H COSY spectrum revealed a long-range coupling (J = 3 Hz) of this methine proton with the glucose C-1 proton. In the HMBC spectrum (Figure 1), both of these two protons were correlated with the ketone carbon signal (Cp-3) and the carbon signals due to the tetrasubstituted double bond (Cp-4 and -5). In addition, long-range H−C couplings of the benzyl methine proton signal (Cp-1) were also observed with three aromatic carbons, the oxygen-bearing quaternary carbon (Cp-2), and the nonconjugated ester carboxyl carbon (Cp-6), which also correlated with the methoxyl proton. The observation of these correlations permitted us to construct a cyclopentenone ring possessing a methoxycarbonyl group as shown in Figure 1, and this was consistent with the molecular weight (966 dalton) revealed by the negative ion FABMS, which showed the $[M - H]^-$ peak at m/z 965.

The CD spectrum of **1** showed a positive Cotton effect at 239 nm and a negative one at 267 nm, indicating that the atropisomerism of the HHDP group had the *S*-configuration.[18] The NOESY spectrum showed the cross-peaks between H-1 and H-2, and between H-2 and H-3, and no proton was correlated with the benzyl methine proton (Cp-1). On the assumption that this compound was derived from **4**, examination using a Dreiding model and computer-aided molecular modeling (CAChe system) indicated that the benzyl methine proton (Cp-1) must be β oriented for construction of both six-membered (including glc-1, -2 and Cp-4, -5) and 10-membered lactone rings (including

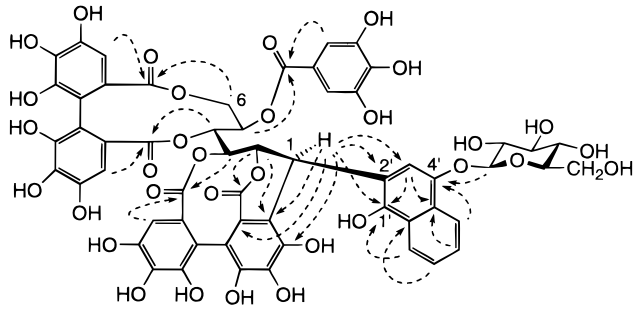
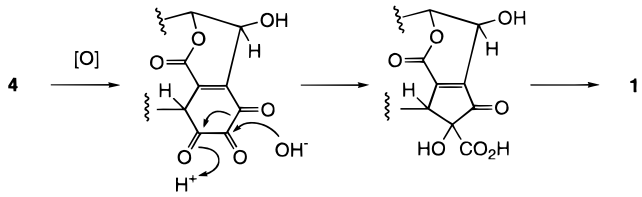


Figure 2. Selected HMBC correlations (H→C) observed for **2**.

Scheme 1. Biogenesis of Rhoipteleanin H (**1**).

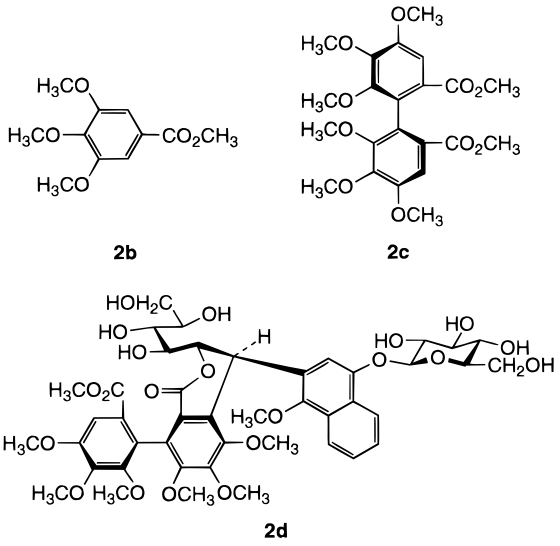


glc-2, -3 and Cp-1, -5). Configuration of the quaternary carbon (Cp-2) of the cyclopentenone ring could not be confirmed clearly; however, the absence of NOE between the Cp-1 proton and the methoxyl group suggested an α orientation of the methoxycarbonyl group.

From these results, the structure of rhoipteleanin H was proposed to be represented by the formula **1**. This compound was presumed to be formed by oxidation of a pyrogallol ring attached to the glucose C-1 of **4** followed by benzylic acid-type rearrangement and methylation (Scheme 1).

Rhoipteleanin I (**2**) showed a dark blue coloration with 1% $FeCl_3$ reagent. The ^1H and ^{13}C NMR spectra (Tables 1 and 2) exhibited aliphatic signals arising from a glycosidically linked *β*-glucopyranose with $^4C_1$-conformation and a fully acylated polyalcohol moiety. The signals due to the polyalcohol moiety were similar to those of the stachyurin unit in stenophyllanin B (**5**), a complex tannin isolated from *Quercus* species (Fagaceae),[19] suggesting the presence of a C-1 substituted stachyurin unit in **2**. This was supported by the appearance of the signals due to five ester carbonyl carbons and five pyrogallol-type aromatic rings in the ^{13}C NMR spectrum and confirmed by the HMBC correlations (Figure 2) between the oxygen-bearing aliphatic protons and the ester carbonyl carbons, and between the ester carbonyl carbons and aromatic protons.

The remaining 10 aromatic carbon signals suggested the presence of a dioxygenated naphthalene moiety. The coupling pattern of the aromatic protons [one singlet at *δ* 6.79, two broad doublets at *δ* 8.24 and 8.26 (d, $J = 9$ Hz), and two double-triplets at *δ* 7.41 and 7.47 ($J = 1$ and 9 Hz)] indicated that this naphthalene moiety is 1,2,4-trisubstituted. The negative FABMS spectrum of **2** showed an $[M - H]^-$ ion peak at *m/z* 1239, and a methyl ether **2a** obtained by methylation with Me_2SO_4–K_2CO_3 exhibited the $[M + Na]^+$ ion peak at *m/z* 1487 in the positive FABMS. This result suggested that there is one phenolic hydroxyl group on the naphthalene moiety in addition to 15 phenolic hydroxyl groups of the pyrogallol rings in **2**. The positions of the hydroxyl and glucopyranosyl groups were determined to be located at C-1′ and C-4′, respectively, on the basis of the HMBC experiment shown in Figure 2. Furthermore, because the H-1 of the stachyurin unit was correlated to the C-1′, C-2′, and C-3′ of the naphthalene moiety (Figure 2), the location of stachyurin unit was determined to be at the C-2′ position of the naphthalene moiety.



The atropisomerism of the HHDP groups in **2** was chemically confirmed by alkaline hydrolysis (2% NaOMe–MeOH) of **2a**, yielding methyl trimethoxybenzoate (**2b**), dimethyl hexamethoxydiphenate **2c** ($[\alpha]_D$ −32.5°, $CHCl_3$),[20] and **2d**. The negative specific rotation value of **2c** indicated the *S*-configuration of the biphenyl bond. In addition, the atropisomerism of the *C*-substituted HHDP (BPH) group was also deduced to be in the *S*-series from the observation of a positive Cotton effect at 237 nm and a negative one at 264 nm in the CD spectrum of **2**. Thus, the structure ofrhoipteleanin I was established to be as shown in formula **2**.

Although complex tannins comprising a *C*-glycosidic ellagitannin unit and a flavan-3-ol unit were found in the Juglandaceae,[21] Fagaceae,[19,22] Myrtaceae,[23] Combretaceae,[24] and Theaceae,[25] rhoipteleanin I (**2**) represents a new type of tannin in which a naphthalene glycoside unit is connected to an ellagitannin unit through a carbon–carbon linkage.

Rhoipteleanin J (**3**) was also characterized as an ellagitannin by coloration with $FeCl_3$ and $NaNO_2$–AcOH reagent. In the aliphatic region of the ^1H NMR spectrum, a methine singlet (*δ* 4.48) and two sets of signals arising from two polyalcohol moieties (units A and B) were observed (Table 1). The ^1H and ^{13}C NMR (Table 2) spectral comparison showed that chemical shifts and coupling pattern of the unit A were similar to those of **4**, except for the small $J_{H-4,H-5}$ value. The signals due to the remaining polyalcohol moiety (unit B) seem to be related to those of psidinin C (**6**).[23] In the aromatic region, the ^1H NMR spectrum exhibited a two-proton singlet (*δ* 7.09) due to a galloyl group and seven one-proton aromatic singlets, and the ^{13}C NMR spectrum revealed the presence of eight pyrogallol rings along with 10 ester carbonyl signals. These spectroscopic data indicated that **3** is a dimeric ellagitannin consisting of two *C*-glycosidic ellagitannin units. This was supported by the negative ion FABMS, which showed the $[M-H]^-$ peak at *m/z* 1823.

Partial hydrolysis of **3** in hot water afforded casuariin (**7**),[11,12] indicating the presence of a casuarinin unit (unit A) in the molecule of **3**. The remaining part of the molecule (unit B) was determined by following spectroscopic observation: first, analysis of the ^{13}C NMR and HMBC spectra showed a galloyl group at the glucose C-5′ position and an HHDP group at the C-4′ and C-6′ positions (Figure 3). Next, the ^{13}C NMR chemical shifts of the signals due to a methine (Cp-1), a tetrasubstituted double bond (Cp-2, -3), a conju-

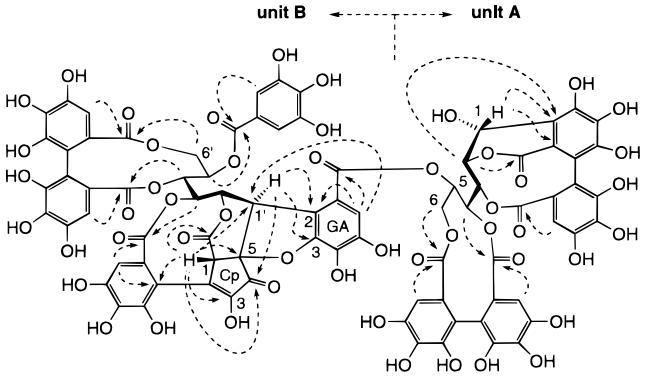


Figure 3. Selected HMBC correlations (H→C) observed for **3**.

gated ketone (Cp-4), and an aliphatic quaternary carbon (Cp-5) were almost identical to those of the cyclopentenone ring of **6** (Table 2). Presence of the partial structure similar to that of **6** was comfirmed by the HMBC experiment (observed at J_{CH} = 4, 6, 8, 10, and 12 Hz, Figure 3): a long-range correlation of the methine (δ 4.48, Cp-1) with the glucose C-1′ (unit B) revealed connectivitiy of the cyclopentenone ring to glucose C-1′. In addition, a series of correlations through the glucose H-3′ (unit B)−3′-ester carbonyl carbon (δ 166.6)−an aromatic proton of a pyrogallol ring (δ 6.55)−an aromatic carbon (δ 111.0)−the Cp-1 proton−2′-ester carbonyl carbon (δ 168.3) confirmed the presence of a macrocyclic lactone ring. The remaining galloyl residue (GA) was shown to be attached to the glucose C-1′ (unit B) through a C−C bond, because the glucose H-1′ (unit B) was correlated with C-2 (δ 124.1) and C-3 (δ 148.5) of the galloyl group (GA), and an aromatic proton (δ 7.20) was coupled with the glucose C-1′ (^4J) and a carboxyl group (δ 165.6) (Figure 3). An ether linkage between the C-3 hydroxy group of the galloyl residue and the quaternary carbon (Cp-5) of the cyclopentenone ring was deduced from the appearance of the C-3 signal of the galloyl residue at lower field (δ 148.5) compared to that of usual galloyl group (δ 145.7). Furthermore, the orientation of the glucose H-1 and methine proton (Cp-1) of the cyclopentenone ring was presumed to be α and β, respectively, because the NOESY spectrum showed NOE correlation between glucose H-1 and H-3 and no correlation peaks with the Cp-1 proton. Computer-aided molecular modeling indicated that the alternative configuration of the Cp-1 methine carbon, although it was a distorted structure with strong strain, required the NOE between the methine proton and both of the glucose H-1 and H-2 (2.2−2.5 Å).

Because partial hydrolysis of **3** gave **7** and the ^{1}H NMR chemical shift indicated acylation of the C-5 hydroxyl group of the casuarinin unit (unit A), it was strongly suggested that the carboxyl group of the galloyl residue attached to the C-1′ position of the unit B was linked to the C-5 hydroxyl group of the unit A. In addition, atropisomerism of three biphenyl bonds was determined to be all *S* in configuration from appearance of a large positive Cotton effect at 236 nm and a negative one at 267 nm in the CD spectrum. On the basis of these results, the structure of rhoipteleanin J was proposed as that shown in formula **3**.

In our previous paper,[7] the establishment of the order Rhoipteleales (comprising Rhoipteleaceae as the only family) and the taxonomic affinities of this order to Juglandales, Fagales, and Myricales were proposed chemotaxonomically. The isolation of the characteristic ellagitannins, rhoipteleanins H−J, from this plant provides further support for the systematic position of this monotypic family. Because juglone-related glucosides are well known as the chemotaxonomic marker of Juglandaceae, the occurrence of rhoipteleanin I (**2**) having a juglone-related glucoside moiety in the molecule also supported the relationship between the Rhoipteleaceae and Juglandaceae, although the glycosides with nonconjugated form have not been isolated from this plant so far.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. Column chromatography was performed with Sephadex LH-20 (25−100 μm, Pharmacia Fine Chemical Co. Ltd.), MCI-gel CHP 20P (75−150 μm, Mitsubishi Chemical Industries, Ltd.), Bondapak ODS (Waters), and Chromatorex ODS (Fuji Silysia). Thin-layer chromatography was performed on precoated Si gel 60 F_{254} plates (0.2 mm thick, Merck) with C_6H_6−HCOOEt−HCOOH (1:7:1 or 1:7:2 v/v) and precoated cellulose F_{254} plates (0.1 mm thick, Merck) with 2% HOAc, and spots were detected by UV illumination and by spraying with 2% ethanolic $FeCl_3$ reagent. Analytical HPLC was performed on a Tosoh apparatus equipped with a CCPM solvent delivery system, UV-8000 spectrometer (280 nm) and a Cosmosil 5C_{18}-AR (Nacalai Tesque Inc.) column (4.6 mm i.d. × 250 mm) (mobile phase, CH_3CN−50 mM H_3PO_4, gradient elution from 5 to 30% CH_3CN for 30 min; flow rate, 0.8 mL/min). The CD spectra were measured with a JASCO J-720w apparatus. Negative FABMS were recorded on a JEOL JMX DX-303 spectrometer with glycerol as a matrix. ^{1}H and ^{13}C NMR spectra were obtained with Varian Unity plus 500 and Varian Gemini 300 spectrometers operating at 500 and 300 MHz for ^{1}H, and 125 and 75 MHz for ^{13}C, respectively; chemical shifts are reported in parts per million on the δ scale with TMS as the internal standard, and coupling constants are in Hertz. HMQC (J_{CH}=140 Hz), HMBC ($^nJ_{CH}$ optimized for 4, 6, 8, 10, and 12 Hz) and NOESY (mixing time 0.50 s) experiments were performed using standard Varian pulse sequences. Computer-aided molecular modeling was done by Mechanics version 3.7 of CAChe system (CAChe Scientific).

Plant Materials. Fruits and bark of *R. chiliantha* were collected in Huaping, Guangxi, China. A voucher specimen has been deposited in the Laboratory of Plant Chemotaxonomy, China Pharmaceutical University, Nanjing.

Isolation. The air-dried fruits (495 g)[6] were extracted with MeOH and then 70% Me_2CO. The extracts were combined, and the organic solvent was evaporated under reduced pressure. The resulting aqueous solution was partitioned with Et_2O and EtOAc successively to afford the Et_2O extract (24.0 g), the EtOAc extract (9.0 g), and the aqueous extract (26.4 g). The H_2O layer was chromatographed on MCI-gel CHP 20P [0−100% MeOH−Me_2CO−H_2O (1:1)] to give five fractions: fraction 1 (1.6 g), fraction 2 (3.8 g), fraction 3 (2.0 g), fraction 4 (4.1 g) and fraction 5 (4.9 g). fraction 5 was further subjected to Sephadex LH-20 chromatography [60−100% MeOH and then Me_2CO−H_2O (1:1)] and Bondapak ODS (0−40% MeOH) to afford rhoipteleanin H (**1**) (26 mg).

The air-dried bark (5.7 kg)[2] was extracted with 95% EtOH. The extract (570 g) was partitioned in a manner similar to that described for the fruits to give an Et_2O layer (402 g), EtOAc layer (45 g), and H_2O layer (123 g). The EtOAc layer was subjected to MCI-gel CHP 20P chromatography (0−100% MeOH), and the fractions eluted with 20−60% MeOH were separated by column chromatography over Sephadex LH-20 (40−100% MeOH) to afford casuarinin (**4**)(12.3 g), 1-*O*-galloyl-2,3;4,6-*bis*-(*S*)-HHDP-β-D-glucose (685 mg), and 1,2,3,4,6-penta-*O*-galloyl-β-D-glucose (123 mg). The H_2O layer was subjected to Sephadex LH-20 column chromatography. After washing the column with H_2O, elution of 40−100% MeOH yielded four fractions: fraction 1 (12.4 g), fraction 2 (14.0 g), fraction 3 (8.6 g), and fraction 4 (13.2 g). Fraction 2 was separated by Chromatorex ODS (0−50% MeOH) chromatography to give casuariin (**7**) (194 mg) and pterocarinin A (2.1 g). Chromatography of fraction 3 over MCI-gel CHP 20P (0−50% MeOH) and

Sephadex LH-20 (60−90% MeOH) yielded rhoipteleanins I (**2**) (324 mg) and J (**3**) (40 mg), together with two known ellagitannins, 2,3;4,6-*bis*-(*S*)-HHDP-D-glucose (646 mg) and alienanin B (295 mg).

Rhoipteleanin H (1). tan amorphous powder; $[\alpha]^{15}_D$ −26.7°(c 0.4, MeOH); negative FABMS *m/z* 965 $[M - H]^-$; ^{1}H NMR [500 MHz, $(CD_3)_2CO + D_2O$] δ 7.20 (2H, s, galloyl), 6.91 (1H, s, 4, 6-HHDP−H-3), 6.60 (1H, s, 4, 6-HHDP−H-3′), 6.43 (1H, s, PH-3). ^{13}C NMR [125 MHz, $(CD_3)_2CO+D_2O$] δ 169.1 (HHDP-7′), 168.8 [2C, HHDP-7, C-substituted galloyl (PH)-7], 166.8 (galloyl-7), 163.2 (Cp-7), 146.3 (PH-6), 146.0 (galloyl-3, 5), 145.7 (PH-4), 145.3 × 2, 144.8, 144.6 (HHDP-4, 4′, 6, 6′), 139.8 (galloyl-4), 136.8 (HHDP-5), 136.1 (HHDP-5′), 135.3 (PH-5), 126.4, 125.1 (HHDP-2, 2′), 124.4 (PH-2), 120.2 (galloyl-1), 116.1 (HHDP-1), 115.5 (HHDP-1′), 110.5 (PH-1), 110.2 (galloyl-2, 6), 108.5 (HHDP-3), 107.3, 107.2 (HHDP-3′, PH-3); CD (5.1 × 10^{-5}M, EtOH) $\Delta\epsilon_{267}$ −10.9, $\Delta\epsilon_{239}$ 31.7; *anal.* calcd for $C_{42}H_{30}O_{27}$·9/2 H_2O, C 48.15%; H 3.75%. found: C 48.07%, H 3.67%.

Rhoipteleanin I (2): tan amorphous powder, $[\alpha]^{15}_D$ +22.8° (*c* 0.3, MeOH); negative FABMS *m/z* 1239 $[M - H]^-$, ^{1}H NMR [500 MHz, $(CD_3)_2CO + D_2O$] δ 8.26 [1H, br d, J = 8.9 Hz, naphthalene unit (NP) H-5], 8.24 (1H, br d, J = 9.3 Hz, NP−H-8), 7.47 (1H, dt, J = 1, 9 Hz, NP−H-7), 7.41 (1H, dt, J = 1, 9 Hz, NP−H-6), 7.17 (2H, s, galloyl), 6.79 (1H, s, NP−H-3), 6.77 (1H, s, HHDP-6), 6.60 [1H, s, C-substituted HHDP (BPH)-6′], 6.59 (1H, s, HHDP-3′); ^{13}C NMR [125 MHz, $(CD_3)_2CO + D_2O$] δ 169.4 (BPH-7′), 169.0 (HHDP-7′), 168.5 (HHDP-7), 168.0 (BPH-7), 166.1 (galloyl-7), 147.6 (NP-4), 145.9 (galloyl-3, 5, BPH-4′), 145.4 (NP-1), 145.1, 145.0 (HHDP-4, 4′), 145.9, 144.4, 144.3, 143.2, 143.1 (BPH-6, 6′; HHDP-6, 6′, BPH-4), 139.2 (galloyl-4), 138.6 (BPH-5), 136.6 (HHDP-5), 135.97 (HHDP-5′), 135.7 (BPH-5′), 127.4, 126.7 (HHDP-2, 2′, NP-9, 10), 126.3 (NP-7), 126.0 (NP-6), 124.7 (BPH-2′), 123.5 (NP-2), 122.9 (NP-5), 122.2 (NP-8), 120.8, 120.6 (BPH-2, galloyl-1), 119.3 (BPH-3), 116.5 (BPH-1′), 115.7 (BPH-1), 115.6 (HHDP-1), 115.2 (HHDP-1′), 111.9 (NP-3), 110.0 (galloyl-2, -6), 108.5 (HHDP-3), 107.1 (HHDP-3′), 105.95 (BPH-3′); CD (2.1 × 10^{-5}M, EtOH) $\Delta\epsilon_{264}$ −13.0, $\Delta\epsilon_{237}$ 44.8; *anal.* calcd for $C_{57}H_{44}O_{32}$·$4H_2O$, C 52.14%; H 3.99; found: C 52.00%, H 4.00%.

Methylation of 2. A mixture of **2** (50 mg), Me_2SO_4 (2.0 mL), and anhydrous K_2CO_3 (2.0 g) in dry Me_2CO (20 mL) was heated under reflux for 5 h. The inorganic material was removed by filtration, and the filtrate, after concentration, was applied to a Si gel column. Elution with C_6H_6−Me_2CO (95:5) yielded the hexadecamethylate **2a** (38 mg) as a white amorphous powder; $[\alpha]^{15}_D$ +14.2° (*c* 0.3, $CHCl_3$); positive FABMS *m/z*: 1487 $[M + Na]^+$, 1465 $(M + H)^+$; ^{1}H NMR [300 MHz, $CDCl_3$] δ 7.88, 8.17 (each 1H, d, J = 9 Hz, NP−H-5, 8), 7.24, 7.36 (each 1H, t, J = 9 Hz, NP−H-6, 7), 7.34 (2H, s, galloyl-H), 6.93, 6.71, 6.64, 6.60 (each 1H, s), 5.79 (1H, dd, J = 2, 9 Hz, H-4), 5.46 (1H, dd, J = 3, 9 Hz, H-5), 5.08 (1H, d, J = 2 Hz, H-3), 5.02 (1H, s, H-2), 4.95 (1H, dd, J = 3, 14 Hz, H-6), 4.83 (1H, s, H-1), 4.75 (1H, d, J = 8 Hz, glucopyranose H-1), 4.22 (1H, d, J = 14 Hz, H-6), 4.12, 3.99 (×3), 3.95 (×2), 3.93 (×2), 3.90, 3.87, 3.85, 3.69, 3.64, 3.61, 3.46, 3.44 (each s, total 16 CH_3).

Methanolysis of 2a. Compound **2a** (33 mg) was treated with 2% sodium methoxide in MeOH (5 mL) at room temperature for 6 days. The mixture was neutralized with Amberlite IR120B (H^+ form) and, after concentration, separated by Si gel column chromatography with C_6H_6−Me_2CO (97:3−91:9, v/v) and then $CHCl_3$−MeOH−H_2O (9:1:0.1−8:2:0.2, v/v) to yield methyl trimethoxybenzoate (**2b**) (3 mg), dimethyl (*S*)-hexamethoxydiphenate (**2c**) (5 mg) $[\alpha]^{15}_D$ −32.5° (*c* 0.3, $CHCl_3$), and **2d** (2.4 mg). Compound **2d**: a white amorphous powder, $[\alpha]^{15}_D$ +69.9° (*c* 0.2, MeOH); positive FABMS *m/z* 939 $[M + Na]^+$; ^{1}H NMR [300 MHz, $CDCl_3 + CD_3OD$ (8:1)] δ 8.30, 8.09 (each 1H, d, J = 9 Hz, NP−H-5, 8), 7.56, 7.48 (each 1H, t, J = 9 Hz, NP−H-6, 7), 7.42 (1H, s), 6.62 (1H, s, NP−H-3), 5.32 (1H, d, J = 1 Hz, H-1), 4.90 (1H, d, J = 8 Hz, glucopyranose H-1), 4.74 (1H, dd, J = 1, 7 Hz, H-2), 4.10, 4.03, 3.97, 3.96, 3.84, 3.72, 3.64, 3.60 (each 3H, s, OCH_3).

Rhoipteleanin J (3): tan amorphous powder, $[\alpha]^{15}_D$ −29.0° (*c* 0.2, MeOH); negative FABMS *m/z* 1823 $[M - H]^-$; ^{1}H NMR [500 MHz, $(CD_3)_2CO + D_2O$] δ 7.20 (1H, s, 5-substituted galloyl), 7.09 (2H, s, 5′-galloyl-2, 6), 6.95 (1H, s, 4′, 6′-HHDP-3), 6.91 (1H, s, 4, 6-HHDP-3), 6.62 (1H, s, 4′, 6′-HHDP-3′), 6.57 (1H, s, 4, 6-HHDP-3′), 6.55 (1H, s, 3′-PH-3), 6.44 (1H, s, 2, 3-BPH-3′); ^{13}C NMR [125 MHz, $(CD_3)_2CO + D_2O$] δ 170.4 (2, 3-BPH-7′), 170.0 (4, 6-HHDP-7′), 168.7 (4′, 6′-HHDP-7′), 168.3 (2′-ester carbonyl), 168.2 (4, 6-HHDP-7), 167.1 (4′, 6′-HHDP-7), 166.6 (3′-PH-7), 166.1 (5′-galloyl-7), 165.6 (5-substituted galloyl-7), 165.4 (2, 3-BPH-7), 148.5 (5-substituted galloyl-3), 147.3, 146.4, 145.2, 144.9, 144.46, 144.34, 143.6 (4, 6-HHDP-4, 4′, 6, 6′; 4′, 6′-HHDP-4, 4′, 6, 6′; 3′-PH-4, 6; 5-substituted galloyl-4, 5; BPH-4, 4′, 6, 6′), 145.7 (5′-galloyl-3, 5), 139.3 (5′-galloyl-4), 138.84, 136.81, 136.6, 136.4, 135.7, 135.5, 134.8 (4, 6-HHDP-5, 5′; 4′, 6′-HHDP-5, 5′; 3′-PH-5, BPH-5, 5′), 127.44, 127.36, 126.1, 125.9, 125.5, 124.6 (4, 6-HHDP-2, 2′; 4′, 6′-HHDP-2, 2′; 3′-PH-2, BPH-2′), 124.1 (5-substituted galloyl-2), 120.46, 120.43 (5′-galloyl-1; 2, 3-BPH-2), 117.0, 116.7, 116.2, 116.1, 115.7, 115.6, 115.0 (4, 6-HHDP-1, 1′; 4′, 6′-HHDP-1, 1′; BPH-1, 1′; 5-substituted galloyl-1), 116.7 (2, 3-BPH-3), 112.1 (5-substituted galloyl-6), 111.0 (3′-PH-1), 110.3 (5′-galloyl-2, 6), 109.0 (4′, 6′-HHDP-3), 108.7 (4, 6-HHDP-3), 108.4 (4′, 6′-HHDP-3′), 107.8 (3′-PH-3), 107.3 (4, 6-HHDP-3′), 104.8 (2, 3-BPH-3′); CD (4.1 × 10^{-5}M, EtOH) $\Delta\epsilon_{267}$ −23.3, $\Delta\epsilon_{236}$ 58.8; *anal.* calcd for $C_{81}H_{52}O_{50}$·$8H_2O$; C 49.40%; H 3.48%; found C 49.49%, H 3.42%.

Partial Hydrolysis of 3. A solution of **3** (1 mg) in H_2O (1 mL) was heated (80 °C) for 48 h. HPLC analysis of the mixture showed a peak at t_R 10.1 min, which corresponded to **7**.

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