Isolation and Characterization of Yunnaneic Acids A−D, Four Novel Caffeic Acid Metabolites from *Salvia yunnanensis*

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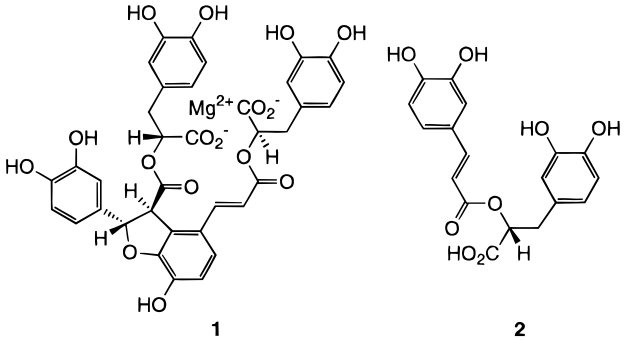
In the course of chemical studies on medicinal plants having uremic toxin-decreasing effects, the novel caffeic acid metabolites yunnaneic acids A−D were isolated from the roots of *Salvia yunnanensis*. Yunnaneic acids C and D were found to be caffeic acid trimers having a bicyclo[2.2.2]octene skeleton, which is biogenetically formed by a Diels−Alder-type addition between rosmarinic acid and caffeic acid. Yunnaneic acid A has a dimeric structure composed of yunnaneic acids C and D, which are linked by formation of a spiroacetal ring. Yunnaneic acid B consists of two molecules of yunnaneic acid C. The structures of the yunnaneic acids were elucidated on the basis of spectroscopic evidence, and their absolute configurations were established by application of the circular dichroic exciton chirality method.

Magnesium lithospermate B (**1**), a caffeic acid tetramer biogenetically derived by oxidative coupling of two molecules of rosmarinic acid (**2**), has been isolated from the roots of *Salvia miltiorrhiza* Bunge (Labiatae) as a compound having an improving effect on renal function in rats with induced renal failure.[1] It seems that **1** increases renal function by improving the renal circulatory state through activation of kallikrein and promotion of prostaglandin E_2 production.[2] In the course of further chemical studies on crude drugs having a uremic toxin-decreasing action, we have isolated four novel caffeic acid metabolites named yunnaneic acids A (**3**), B (**4**), C (**6**), and D (**5**), together with **1** and **2**, from the root of *S. yunnanensis* C. H. Wright (Labiatae). Extensive 2D NMR experiments revealed that compounds **5** and **6** have a bicyclo[2.2.2]octene skeleton formed by Diels−Alder-type addition between **2** and caffeic acid. Furthermore, **3** and **4** were determined to have dimeric structures composed of **5** and **6**, and two molecules of **6**, respectively. These compounds represent novel metabolites in the shikimate pathway in plant metabolism. Herein we report the structural determination of these compounds and briefly discuss their biogenesis.



1 **2**

Results and Discussion

The aqueous Me_2CO extract of the dried roots collected in Yunnan, China, was first subjected to high-porosity-polystyrene gel (MCI−gel CHP 20P) chromatography. Most of the phenolic constituents, however, eluted together with sugars and inorganic substances. An attempt to fractionate with Sephadex LH-20 also failed. The reason for this behavior was thought to be the formation of salts, as noted for lithospermic acid B from *S. miltiorrhiza*.[1] Compared to *S. miltiorrhiza*, the composition of the extract was too complex to isolate each component as its salt; hence, the phenolic fraction was first acidified prior to separation and adsorbed on a Sephadex LH-20 column. After washing the column with H_2O to remove inorganic material, sugars, and so forth, phenolic substances were eluted with aqueous MeOH. No significant change was observed in the HPLC profiles (reversed-phase Si gel with CH_3CN−50 mM H_3PO_4 as eluent, 280 nm) of the original extract and the phenolic fraction obtained after acidification. The fractions thus obtained were repeatedly chromatographed over MCI−gel CHP 20P, Sephadex LH-20, and reversed-phase Si gels (Chromatorex ODS and Bondapak C_{18}) to give yunnaneic acids A (**3**), B (**4**), C (**6**), and D (**5**), along with lithospermic acid B (**1**) and rosmarinic acid (**2**).

Yunnaneic acid A (**3**) was obtained as a tan amorphous powder and gave a greenish blue coloration characteristic of catechol with 2% ethanolic $FeCl_3$ on TLC. The ^{1}H-NMR spectrum showed two pairs of doublets (J = 16 Hz) due to *trans*-double bonds (A-7,[3] A-8, B-7, and B-8) conjugated with a carbonyl group, and aromatic proton signals attributable to four catechol rings (Table 1). The appearance of signals due to two oxygen-bearing methines at δ 5.26 (A-8″) and 5.19 (B-8″), and two benzylic methylenes in the range of δ 2.99 to 3.15 was analogous to those of **1**, suggesting the presence of two dihydroxyphenyllactic acid moieties. This was comfirmed by acid hydrolysis yielding (*R*)-3-(3,4-dihydroxyphenyl)lactic acid.[4] The ^{13}C-NMR spectrum (Table 1) exhibited six carboxyl carbon signals, two of which were indicated to be conjugated with above-mentioned double bonds from their chemical shifts [δ 166.9 (A-9) and 166.3 (B-9)]. In the HMBC spectrum,

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Table 1. ^{1}H- and ^{13}C-NMR Assignments and HMBC (8 Hz) Correlations of Yunnaneic Acid A (**3**) (in Me_2CO-d_6)

position[a]	δ_H[b]	δ_C	HMBC ($^{13}C \rightarrow {}^1H$)[d]	position[a]	δ_H[b]	δ_C	HMBC($^{13}C \rightarrow {}^1H$)[d]
A-1		141.9	A-2, A-5, A-8, A-8′	B-1		137.9	B-2, B-5, B-7, B-8, B-8′
A-2	3.91 (br s)	44.9	A-6, A-7, A-8′, A-3-OH	B-2	3.96 (dd, 1.5, 2)	50.6	B-6, B-7, B-8′
A-3		109.1	A-2, A-4, A-5, A-6, A-8′, A-3-OH	B-3		207.5	B-2, B-5, B-6, B-8′
A-4	4.37 (d, 4)	88.1	A-2, A-5, A-6, A-7′	B-4		103.0	B-2, B-5, B-6, B-7′, A-4
A-5	3.10[e]	45.5	A-6, A-7′	B-5	2.67 (dd, 2, 7)	50.9	B-7′, B-8′
A-6	6.62 (br d, 6)	139.0	A-2, A-4, A-5, A-7, A-8, A-7′	B-6	6.79 (br d, 7)	140.6	B-2, B-5, B-7, B-7′
A-7	7.48 (d, 16)	143.6	A-2, A-6	B-7	7.40 (d, 16)	141.5	B-2, B-6
A-8	6.27 (d, 16)	116.9	A-7	B-8	6.25 (d, 16)	118.7	B-7
A-9		166.9	A-7, A-8, A-8″	B-9		166.3	B-7, B-8, B-8″
A-1′		136.9	A-5′, A-7′, A-8′	B-1′		135.4	B-5, B-5′, B-7′, B-8′
A-2′	6.67 (d, 2)	115.4	A-6′, A-7′	B-2′	6.55 (d, 2)	114.9	B-6′, B-7′
A-3′		145.6[c]	A-2′, A-5′,-[f]	B-3′		145.7[c]	B-2′, -[f]
A-4′		144.5	A-2′, A-6′,-[f]	B-4′		144.8	B-6′, -[f]
A-5′	6.66 (d, 8)	116.0	[f]	B-5′	6.61 (d, 8)	116.2	B-6′, -[f]
A-6′	6.56 (dd, 2, 8)	119.7	A-2′, A-7′	B-6′	6.37 (dd, 2, 8)	120.2	B-2′, B-5′, B-7′
A-7′	3.46 (br d, 8)	40.7	A-2, A-6, A-2′, A-6′, A-8′	B-7′	3.82 (br dd, 1.5, 7)	43.1	B-2, B-5, B-6, B-2′, B-6′, B-8′
A-8′	2.43 (dd, 2, 8)	50.0	A-2, A-5, A-7′	B-8′	3.04 (dd, 2, 7)	51.2	B-2, B-7′, B-8′
A-9′		173.4	A-2, A-7′, A-8′	B-9′		173.6	B-7′, B-8′
A-1″		128.8	A-5″, A-7″, A-8″	B-1″		128.9	B-5″, B-7″, B-8″
A-2″	6.85 (d, 2)	117.5	A-6″, A-7″	B-2″	6.80 (d, 2)	117.3	B-6″, B-7″
A-3″		145.6[c]	A-2″, A-5″,-[f]	B-3″		145.7[c]	[f]
A-4″		144.8	A-2″, A-5″, A-6″	B-4″		144.8	[f]
A-5″	6.72 (d, 8)	116.0	[f]	B-5″	6.71 (d, 8)	116.0	[f]
A-6″	6.67 (dd, 2, 8)	121.7	A-2″, A-7″	B-6″	6.64 (dd, 2, 8)	121.6	B-2″, B-7″
A-7″	3.06−3.15 (m)	37.4	A-2″, A-6″, A-8″	B-7″	2.99 (dd, 8, 14) 3.06−3.15 (m)	37.3	B-2″, B-6″, B-8″
A-8″	5.26 (dd, 6, 7)	74.1	A-7″	B-8″	5.19 (dd, 4, 8)	74.0	B-7″
A-9″		171.2	A-7′, A-8″	B-9″		170.9	B-7″, B-8″
A-3-OH	5.00 (s)						

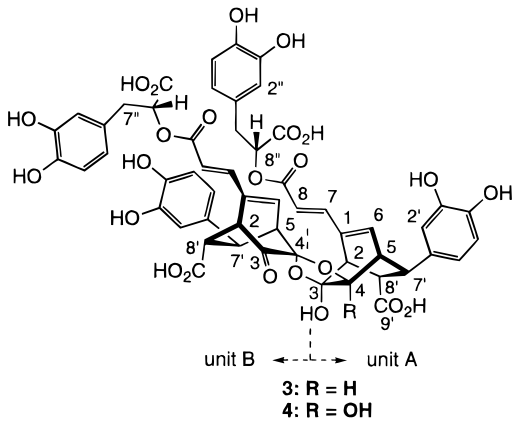
[a] Numbering of the carbons is based on caffeic acid residue. [b] ^{1}H chemical shift values (δ ppm from TMS) followed by multiplicity and the coupling constants (J in Hz) in parentheses. [c] Assignments may be interchanged. [d] Correlation from C to H observed in the HMBC experiment. [e] Overlapped with A-7″ signals. [f] Crosspeaks are overlapped.

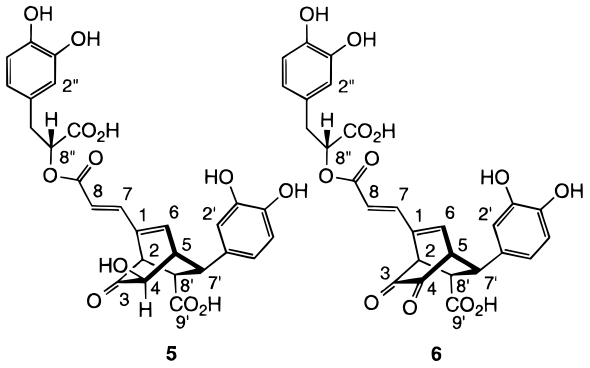
both of the conjugated carboxyl carbons were correlated with the oxygen-bearing methine protons (A-8″ and B-8″) of the dihydroxyphenyllactic acid moieties (Table 1), indicating that these α, β-unsaturated carboxyl groups are attached to lactic acid moieties through ester linkages.

One of the olefinic doublets (δ 7.48, J = 16 Hz, A-7), attributable to the β proton of the α,β-unsaturated carboxyl group (A-9), showed a three-bond long-range correlation with aliphatic (δ 44.9, A-2) and olefinic (δ 139.0, A-6) methine carbons. The allylic coupling between these methine protons (δ 3.91 and 6.62, respectively) was shown by an ^{1}H−^{1}H COSY experiment. In addition, the appearance of a spin system consisting of five methine protons (A-2, A-8′, A-7′, A-5, and A-6) showed the presence of a cyclohexene ring. Furthermore, the methine proton at δ 3.10 (A-5) was vicinally coupled with the oxygen-bearing methine proton at δ 4.37 (A-4), and these two methine proton signals as well as signals at δ 3.91 (A-2) and 2.43 (A-8′) were all correlated with an acetal carbon signal (δ 109.1, A-3) in the HMBC spectrum. These observations revealed the occurrence of the bicyclo[2.2.2]octene structure in the molecule. The location of a carboxyl group (A-9′) at A-8′ position and a catechol ring at A-7′ position was deduced from the HMBC correlations (Table 1). These spectral findings consequently showed the occurrence of the structural unit A of **3**. The relative configuration of unit A was unambiguously determined by analyzing the NOESY spectra measured in pyridine-d_5 and in Me_2-CO-d_6 (Table 3), which showed correlations between A-8 and A-8′, between A-2′ (6′) and A-8′, between A-6 and A-2′, between A-4 and A-7′, and between A-4 and hydroxyl proton at A-3.

The correlations of the remaining proton and carbon signals in the ^{1}H−^{1}H COSY and HMBC spectra (Table 1) revealed the presence of the unit B, which has an analogous structure to the unit A, except for the occurrence of a carbonyl group (δ 207.5, B-3) and an acetal carbon (δ 103.0, B-4) in place of the acetal (A-3) and the oxygen-bearing methine (A-4) in unit A. The linkage between the units A and B was substantiated by observation of an HMBC correlation between the methine proton at A-4 and the acetal carbon B-4 (Table 1). Taking the molecular weight indicated by negative ion FABMS [m/z: 1077 $(M - H)^-$] into account, this three-bond long-range coupling suggested the formation of the cyclic acetal at B-3 carbon with the oxygen atoms located at A-3 and A-4 positions. This was confirmed by observation of interunit NOEs between A-6 and B-5, and between A-7 and B-5; furthermore, the configuration of the acetal carbon B-4 was also determined.

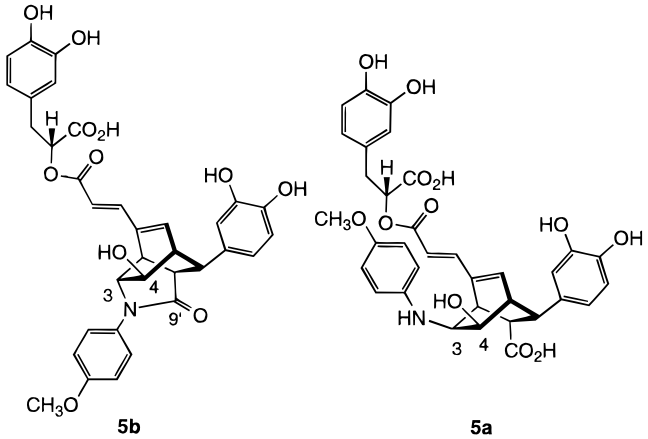
On treatment with dilute HCl, compound **3** liberated yunnaneic acids D (**5**) and C (**6**), which were also isolated from the extract. Yunnaneic acid D (**5**) showed an $[M - H]^-$ ion peak at m/z 539 in its negative ion FABMS spectrum, which coincided with the mass of unit A (3-ketone form) of **3**. The proton signals also corresponded well with those of the unit A of **3**. The other product, yunnaneic acid C (**6**), exhibited an $[M - H]^-$ peak at m/z 537 (3,4-diketone form) indicating that this product originated from unit B. The appearance of the ion peaks at m/z 569 and m/z 629 suggested the occurrence of an acetal form of **6** with MeOH and glycerol used as solvent and matrix. Despite a homogeneous spot on the TLC plate, **6** showed a broad peak on analysis by HPLC. Its ^{1}H- and ^{13}C-NMR spectra were also complicated and could not be interpreted except for the signals arising from 3-(3,4-dihydroxyphenyl)lactic acid moiety. These phenomena were considered to be caused by hydration of two neighboring carbonyl groups; therefore, a quinoxaline derivative **6a** was



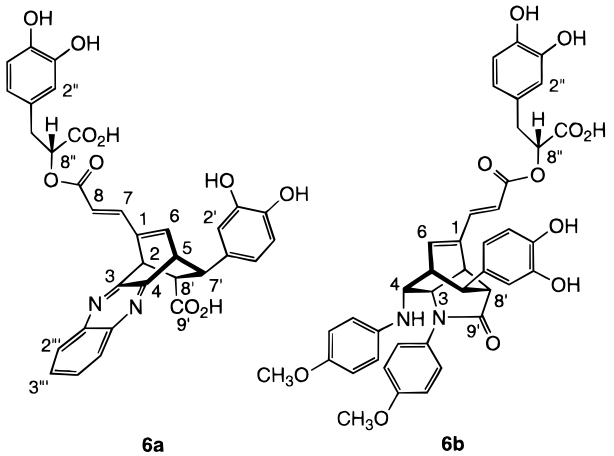


5 **6**

synthesized by condensation with *o*-phenylenediamine. Compound **6a** exhibited well separated signals in its ^{1}H- and ^{13}C-NMR spectra, which were consistent with the structure of unit B of **3**.



5b **5a**



6a **6b**

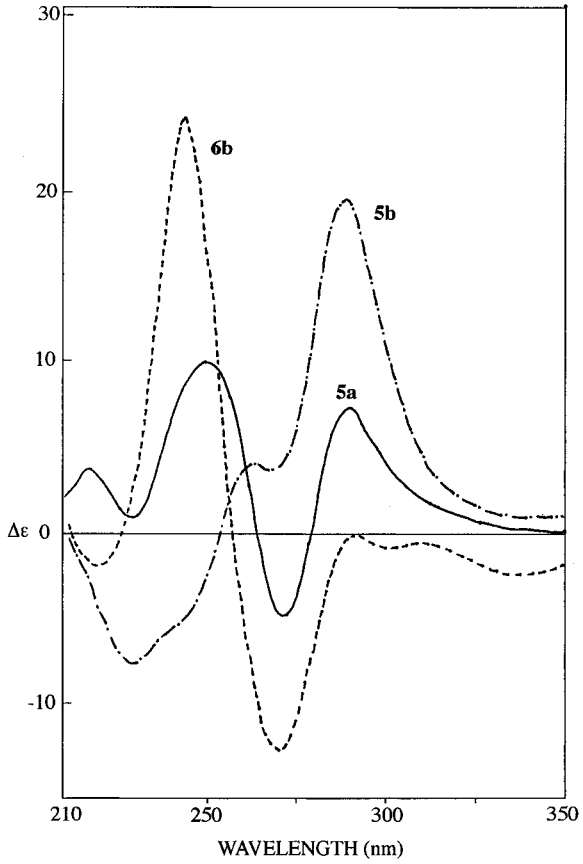
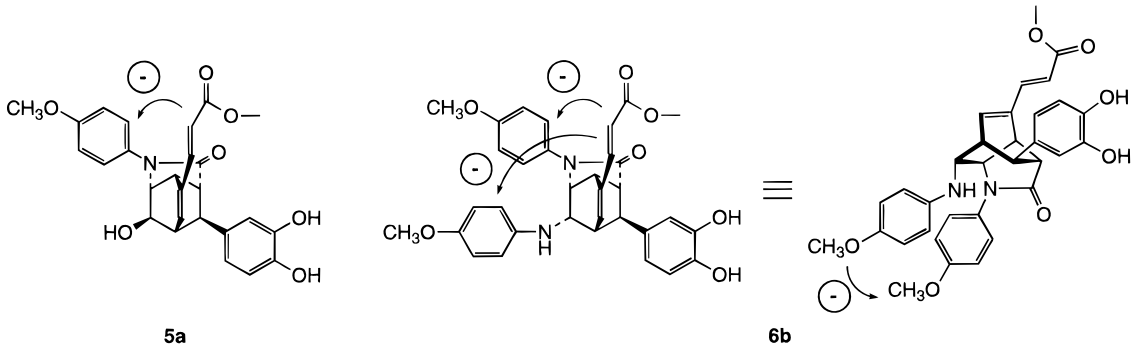


Figure 1. CD spectra of **5a**, **5b**, and **6b**.

The determination of the absolute configuration of **5** and **6** was achieved by application of the circular dichroic (CD) exciton chirality method[5] to *p*-methoxyphenylamino derivatives **5a**, **5b**, and **6b**. These derivatives were obtained by condensation with *p*-anisidine followed by reduction with $NaBH_3CN$. The presence of a lactam ring in **5a** and **6b** was shown by FABMS, and that of **6b** was further confirmed by the HMBC spectrum, which showed a ^3J correlation between H-3 and C-9. Relative configurations of C-3 and C-4 were determined by comparison of the coupling constants between H-3 and H-4 [**5a**: $J_{3,4} = 0$ Hz (*trans*); **5b**: $J_{3,4} = 8$ Hz (*cis*); **6b**: $J_{3,4} = 7.5$ Hz (*cis*)] with those of related compounds.[6] Compound **5a** showed a split CD curve with a negative first Cotton effect at 272 nm and a positive second Cotton effect at 250 nm (Figure 1). On the other hand, **5b** did not show such a split curve. Because the position of this curve is in agreement with the λ max of the *p*-methoxyphenylamino residues (255 nm) and $\alpha, \beta; \gamma, \delta$-unsaturated ester (275 nm), the split CD curve of **5a** is ascribed to chiral interaction between these two chromophores. This observation indicates that the configuration of these two chromophores is counterclockwise. Compound **6b** also exhibited a strong split CD curve with negative first Cotton effect at 271 nm and positive second Cotton effect at 244 nm. This CD curve is accounted for by an additivity relation between three interacting chromophores (Figure 2).[7] On the basis of these results, the absolute structure of yunnaneic acids A, C, and D were concluded to be as shown in formulae **3**, **5**, and **6**, respectively.

Yunnaneic acid B (**4**) showed an $[M - H]^-$ peak at *m*/*z* 1093, which was 16 mass units larger than that of **3**. The ^{1}H- and ^{13}C-NMR signals and HMBC correla-



5a **6b**

Figure 2.

Table 2. ^{1}H- and ^{13}C-NMR Assignments and HMBC Correlations of Yunnaneic Acid B (**4**) (in Me_2CO-d_6 + D_2O)

position[a]	δ_H[b]	δ_C	HMBC ($^{13}C \rightarrow {}^1H$)[d]	position[a]	δ_H[b]	δ_C	HMBC ($^{13}C \rightarrow {}^1H$)[d]
A-1		141.6	A-2, A-5, A-8, A-8′	B-1		137.7	B-5, B-7, B-8, B-8′
A-2	4.00 (t, 2)	46.2	A-6, A-7, A-8′	B-2	3.96 (br s)	51.0	B-7, B-8′
A-3		105.8	A-2, A-5, A-8′	B-3		206.3	B-2, B-5, B-8′
A-4		106.3	A-2, A-5, A-7′	B-4		101.6	B-2, B-5, B-7′
A-5	3.10[e]	50.5	A-6	B-5	2.68 (dd, 2, 7)	51.0	B-7, B-7′, B-8′
A-6	6.71 (br d, 6)	139.8	A-2, A-7′	B-6	6.74[e]	140.6	B-5, B-7, B-7′
A-7	7.49 (d, 16)	143.7		B-7	7.40 (d, 16)	141.7	B-8
A-8	6.35 (d, 16)	117.3		B-8	6.24 (d, 16)	118.7	
A-9		167.0	A-7, A-8, A-8″	B-9		166.5	B-7, B-8
A-1′		137.0	A-5′, A-7′, A-8′	B-1′		135.3	B-5, B-5′, B-7′, B-8′
A-2′	6.73 (d, 2)	115.5	A-7′	B-2′	6.54 (br s)	115.0	B-7′
A-3′		145.6[c]	[f]	B-3′		145.6[c]	[f]
A-4′		144.8	[f]	B-4′		144.5	B-2′, [f]
A-5′	6.69 (d, 8)	116.0	[f]	B-5′	6.62 (d, 8)	116.2	[f]
A-6′	6.56 (dd, 2, 8)	120.0	A-5′, A-7′	B-6′	6.33 (br s)	120.3	B-2′, B-7′
A-7′	3.95 (d, 8)	40.3	A-2, A-2′, A-6′, A-8′	B-7′	3.71 (dd, 2, 7)	42.6	B-2, B-2′, B-6′, B-8′
A-8′	2.49 (dd, 2, 8)	50.3	A-2, A-5, A-7′	B-8′	3.04 (dd, 3, 7)	50.5	B-5, B-7′
A-9′		174.0	A-7′, A-8′	B-9′		174.2	B-7′, B-8′
A-1″		128.7	A-5″, A-7″, A-8″	B-1″		128.9	B-8″
A-2″	6.88 (d, 2)	117.5	A-6″, A-7″	B-2″	6.83 (d, 2)	117.5	B-6″, B-7″
A-3″		145.7[c]	[f]	B-3″		145.7[c]	[f]
A-4″		144.8	[f]	B-4″		144.8	[f]
A-5″	6.75 (d, 8)	116.0	[f]	B-5″	6.73 (d, 8)	116.0	[f]
A-6″	6.69 (dd, 2, 8)	121.7	A-2″, A-7″	B-6″	6.65 (dd, 2, 8)	121.6	B-7″
A-7″	3.08−3.17 (m)	37.4	A-2″, A-6″, A-8″	B-7″	3.00 (dd, 8, 14) 3.08−3.17 (m)	37.4	B-2″, B-6″, B-8″
A-8″	5.29 (dd, 6, 7)	74.3	A-7″	B-8″	5.21 (dd, 4, 9)	74.2	B-7″
A-9″		171.4	A-7′, A-8″	B-9″		171.1	B-7″, B-8″

[a] Numbering of the carbons is based on caffeic acid residue. [b] ^{1}H chemical shift values (δ ppm from TMS) followed by multiplicity and the coupling constants (J in Hz) in parentheses. [c] Assignments may be interchanged. [d] Correlation from C to H observed in the HMBC experiment. [e] Overlapped with other signals. [f] Crosspeaks are overlapped.

tions (Table 2) were closely related to those of **3**, except for the appearance of an acetal carbon (δ 106.3) in place of the oxygen-bearing methine carbon of **3** (δ 88.1, A-4). This acetal carbon was assigned to A-4 on the basis of its HMBC correlations with the methine protons at A-2, A-5, and A-7′ positions. These results suggested that **4** was composed of two molecules of yunnaneic acid C (**5**), and this was confirmed by treatment of **4** with *o*-phenylenediamine to yield **6a**. The NOESY spectrum (Table 3) showed interunit correlations similar to those observed in the spectrum of **3**, confirming the stereochemistry of the spiroacetal ring. Thus, the structure of yunnaneic acid B was concluded to be represented by the formula **4**.

Yunnaneic acids represent novel metabolites of the shikimate pathway. The bicyclo[2.2.2]octene structure of yunnaneic acids C(**5**) and D(**6**) strongly suggested a biogenesis as shown in Scheme 1: the Diels−Alder addition between one of the cathecol rings of rosmarinic acid (**2**) and the double bond of caffeic acid would afford **6**. On the other hand, similar addition between the *ortho*-quinone and caffeic acid would give **5**. Furthermore, **3** and **4** are apparently generated by intermolecular spiroacetal formation between **5** and **6**, and two molecules of **5**, respectively.

Experimental Section

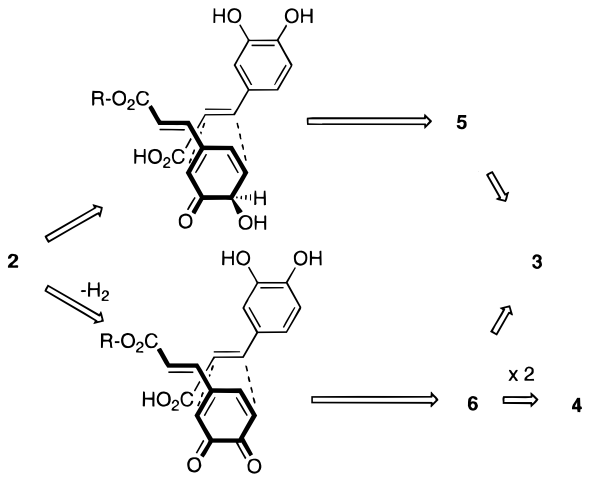
General Experimental Procedures. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. Analytical HPLC was performed on a Tosoh apparatus equipped with a CCPM solvent delivery system, UV-8000 spectrometer (280 nm) and a Cosmosil 5C_{18}-AR (Nacalai Tesque, Inc.) column (4.6 mm i.d. × 250 mm) (mobile phase, CH_3CN−50 mM H_3PO_4, gradient elution from 15 to 35% CH_3CN for 40 min; flow rate, 0.8 mL/min). Column chromatographies were performed with Sephadex LH-20 (25−100 μm, Pharmacia Fine Chemical Co., Ltd.), MCI−gel CHP 20P (75−150 μm, Mitsubishi Chemical Industries, Ltd.), and Chromatorex ODS (Fuji Silysia). TLC were performed on precoated Si gel 60 F_{254} plates (0.2-mm thick, Merck) with C_6H_6−HCOOEt−HCOOH (1:7:1, 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 2% ethanolic $FeCl_3$ reagent. The IR absorption spectra were obtained with a JASCO IR-810

Table 3. NOESY Correlations of Yunnaneic Acids A (**3**) and B (**4**) (500 MHz, in pyridine-d_5)

yunnaneic acid A (**3**)				yunnaneic acid B (**4**)			
proton[a]	NOE correlation	proton[a]	NOE correlation	proton[a]	NOE correlation	proton[a]	NOE correlation
A-2	A-7, A-8, A-8′	B-2	B-7, B-8, B-8′	A-2	A-7, A-8, A-8′	B-2	B-7, B-8, B-8′
A-4	A-5, A-7′						
A-5	A-4. A-6, A-2′, A-6′, A-7′	B-5	B-2′, B-6′, B-7′, A-6,[c] A-7′[c]	A-5	A-6, A-2′, A-6′, A-7′	B-5	B-2′, B-6′, B-7′, A-6,[c] A-7,[c] A-8′[c]
A-6	A-5, A-2′, B-5[c]	B-6	B-5, B-7	A-6	A-5, A-7, A-8, A-2′, B-5[c]	B-6	B-5, B-7, B-2′, B-6′, A-7[c]
A-7	A-2, A-6, B-5[c]	B-7	B-2, B-6	A-7	A-2, A-6, B-5,[c] B-6,[c] B-7′ [c]	B-7	B-2, B-6, B-8′
A-8	A-2, A-6, A-8′	B-8	B-2, B-6, B-8′	A-8	A-2, A-8′, B-5,[c] B-7′,[c] B-6′ [c]	B-8	B-2, B-8′
A-2′	A-5, A-6, A-7′, A-8′	B-2′	B-5, B-7′, B-8′	A-2′	A-5, A-6, A-7′, A-8′	B-2′	B-5, B-6, B-7′, B-8′
A-5′		B-5′		A-5′		B-5′	B-6′, A-8″
A-6′	A-7′, A-8′	B-6′	B-5, B-7′, B-8′	A-6′	A-5, A-6′, A-7′, A-8′	B-6′	B-5, B-6, B-7′, B-8′, A-8,[c] A-8″ [c]
A-7′	A-4, A-5, A-2′, A-6′, A-8′	B-7′	B-5, B-2′, B-6′, B-8″	A-7′	A-5, A-2′, A-6′, A-8′	B-7′	B-2′, B-6′, B-8′, A-7,[c] A-8[c]
A-8′	A-2, A-8, A-2′. A-6′, A-7′	B-8′	B-2, B-8, B-2′, B-6′, B-7′	A-8′	A-2, A-7, A-8, A-2′, A-6′, A-7′	B-8′	B-2, B-7, B-8, B-2′, B-6′, B-7′
A-2″	A-7″	B-2″	B-7″	A-2″	A-7″, A-8″	B-2″	B-7″, B-8″
A-5″	[d]	B-5″	[d]	A-5″	[d]	B-5″	[d]
A-6″	[d]	B-6″	[d]	A-6″	A-7″, A-8″	B-6″	B-7″, B-8″
A-7″	A-8″	B-7″	B-8″	A-7″	A-2″, A-6″, A-8″	B-7″	B-2″, B-6″, B-8″
A-8″	A-7″	B-8″	B-7″	A-8″	A-2″, A-6″, A-7″, B-5′,[c] B-6′ [c]	B-8″	B-2″, B-6″, B-7″
A-3-OH[b]	A-4						

[a] Numbering of the carbons is based on caffeic acid residue. [b] This correlation was observed in the NOESY spectrum measured at 400 MHz in Me_2CO-d_6. [c] Interunit NOE correlations. [d] Signals are overlapped.

Scheme 1. Biogenesis of Yunnaneic Acids A (**3**), B (**4**), C (**6**), and D(**5**)



spectrophotometer, and UV spectra were recorded using SHIMADZU UV-3100PC spectrophotometer. The CD spectra were measured with a JASCO J-720w apparatus. Negative and positive 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, Varian Unity 400, JEOL GX-400, and Varian Gemini 300 spectrometers operating at 500, 400, and 300 MHz for ^{1}H, and 125, 100, and 75 and 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 8 Hz) and NOESY (mixing time 0.50 s) experiments were performed using standard Varian pulse sequences.

Plant Materials. Roots of *S. yunnanensis* was collected in Kunming, Yunnan, China. A voucher specimen has been deposited in Kunming Plant Research Institute, Yunnan, China.

Isolation. The dried root (1.0 kg) was extracted with 70% aqueous Me_2CO. The extract (300 g) was first subjected to MCI−gel column chromatography (1.5 L) with H_2O containing increasing proportions of MeOH (0 → 100%, stepwise elution with 10% increase at each step) to give four fractions, the first two of which were positive to $FeCl_3$ reagent. The second fraction (19 g) was separated by Sephadex LH-20 (60 → 80% MeOH) and MCI−gel CHP20P (30 → 40% MeOH) chromatography to yield lithospermic acid B (**1**, 1.8 g) and rosmarinic acid (**2**, 0.3 g). The first fraction was concentrated to give an aqueous solution, acidified with 2 M HCl to pH 2 at 0 °C, and applied to a column of Sephadex LH-20 (1.5L) with H_2O. After washing the column with H_2O to elute inorganic material and sugars, the phenolic substances were eluted with aqueous MeOH (20% → 40% → 60%, each 2 L, stepwise elution) to give four fractions. The third fraction was subsequently chromatographed over MCI−gel CHP 20P and Chromatorex ODS with aqueous MeOH (30 → 40%) to afford yunnaneic acids D (**5**, 0.24 g) and C (**6**, 0.61 g). The fourth fraction was subjected to Chromatorex ODS chromatography with H_2O containing increasing amounts of MeOH to yield yunnaneic acids B (**4**, 3.8 g) and A (**3**, 0.67 g).

Yunnaneic acid A (3): tan amorphous powder; $[\alpha]^{25}_D$ +86.1° (*c* 0.5, MeOH); UV-vis (EtOH) λ max (log ϵ) 276 (4.6), 225 sh (4.5); FABMS negative ion (−) *m*/*z* 1077 ([M − H]); ^{1}H NMR (400 MHz, Me_2CO-d_6) Table 1; ^{1}H NMR (500 MHz, pyridine-d_5) δ 7.78 (d, *J* = 15.8 Hz, 1H, A-7), 7.53 (d, *J* = 15.8 Hz, 1H, B-7), 7.47 (d, *J* = 2.1 Hz, 1H, A-2″), 7.43 (d, *J* = 2.1 Hz, 1H, B-2″), 7.29 (d, *J* = 2.1 Hz, 1H, A-2′), 7.28 (d, *J* = 8.0 Hz, 1H, B-5′), 7.20, 7.19, 7.17 (each d, *J* = 8.0 Hz, each 1H, A-5′, A-5″ and B-5″), 7.15 (d, *J* = 2.1, Hz, 1H, B-2′), 7.07 (dd, *J* = 2.1, 8.0 Hz, 1H, A-6″), 7.00 (dd, *J* = 2.1, 8.0 Hz, 1H, B-6″), 6.98 (br d, *J* = 8.0 Hz, 2H, A-6′ and B-6′), 6.69 (br d, *J* = 6.2 Hz, 1H, B-6), 6.62 (br d, *J* = 6.4 Hz, 1H, A-6), 6.53 (d, *J* = 15.8 Hz, 1H, B-8), 6.46 (d, *J* = 15.8 Hz, 1H, A-8), 6.00 (t, *J* = 6.0 Hz, 1H, A-8″), 5.87 (dd, *J* = 4.2, 8.0 Hz, 1H, B-8″), 5.02 (d, *J* = 3.4 Hz, 1H, A-4), 4.48 (br d, *J* = 8.0 Hz, 1H, B-7′), 4.43 (br s, 2H, A-2 and B-2), 4.10 (br d, *J* = 7.8 Hz, 1H, A-7′), 3.58 (m, 3H, A-7″ and B-7″), 3.48 (dd, *J* = 8.0, 14.5 Hz, 1H, B-7″), 3.41 (dd, *J* = 2.1, 7.4 Hz, 1H, B-8′), 3.39 (ddd, *J* = 1.2, 3.4, 6.4 Hz, 1H, A-5), 3.01 (dd, *J* = 1.7, 6.2 Hz, 1H, B-5), 2.87 (dd, *J*

= 2.1, 7.2 Hz, 1H, A-8′); ^{13}C-NMR (100 MHz, Me_2CO-d_6) Table 1; CD (4.1 × 10^{-5} M, EtOH) $\Delta\epsilon_{295}$ 18.5, $\Delta\epsilon_{273}$ 0, $\Delta\epsilon_{254}$ −3.8, $\Delta\epsilon_{241}$ −2.6, $\Delta\epsilon_{228}$ −5.9, $\Delta\epsilon_{216}$ 0.

(*R*)-3-(3,4-Dihydroxyphenyl)lactic Acid from 3. A solution of **3** (45 mg) in 0.25 M H_2SO_4 (5 mL) was heated at 90 °C for 5 h. The mixture was applied to a column of MCI−gel CHP 20P with H_2O to give (*R*)-3-(3,4-dihydroxyphenyl)lactic acid (7 mg): colorless syrup; $[\alpha]^{25}_D$ +10.3° (*c* 0.3, MeOH); ^{1}H NMR (300 MHz, Me_2CO-d_6 + D_2O) δ 6.78 (d, *J* = 2 Hz, 1H, H-2), 6.72 (d, *J* = 8 Hz, 1H, H-5), 6.57 (dd, *J* = 2, 8 Hz, 1H, H-6), 4.27 (dd, *J* = 5, 7 Hz, 1H, H-8), 2.96 (dd, *J* = 5, 14 Hz, 1H, H-7), 2.72 (dd, *J* = 7, 14 Hz, 1H, H-7).

Hydrolysis of 3. A solution of **3** (100 mg) in 0.25 M H_2SO_4 (10 mL) was heated at 90 °C for 1.5 h. The mixture was directly applied to MCI−gel CHP 20P column (1.5 cm i.d. × 15 cm) with H_2O. Elution of the column with aqueous MeOH (40% → 50%) afforded **5** (23.5 mg) and **6** (31.6 mg) together with unreacted **3** (22.3 mg).

Yunnaneic acid D (5): white amorphous powder; $[\alpha]^{25}_D$ +243.4° (*c* 0.7, MeOH); UV-vis (EtOH) λ max (log ϵ) 276 (4.3), 223 (4.3); IR (KBr) 3400, 1735, 1720, 1705, 1690, 1625 cm^{-1}; FABMS negative ion (−) *m*/*z* 539 ([M − H]); ^{1}H NMR (400 MHz, Me_2CO-d_6) δ 7.42 (d, *J* = 16 Hz, 1H, H-7), 6.91 (br d, *J* = 6 Hz, 1H, H-6), 6.84 (d, *J* = 2 Hz, 1H, H-2″), 6.76 (d, *J* = 8 Hz, 1H, H-5″), 6.76 (d, *J* = 8 Hz, 1H, H-5′), 6.76 (d, *J* = 2 Hz, 1H, H-2′), 6.65 (dd, *J* = 2, 8 Hz, 1H, H-6″), 6.55 (dd, *J* = 2, 8 Hz, 1H, H-6′), 6.25 (d, *J* = 16 Hz, 1H, H-8), 5.17 (dd, *J* = 4, 9 Hz, 1H, H-8″), 4.03 (d, *J* = 3 Hz, 1H, H-4), 3.86 (t, *J* = 3 Hz, 1H, H-2), 3.53 (dd, *J* = 2, 6 Hz, 1H, H-7′), 3.30 (ddd, *J* = 2, 3, 6 Hz, 1H, H-5), 3.11 (dd, *J* = 4, 14 Hz, H-7″), 2.99 (dd, *J* = 8, 14 Hz, 1H, H-7″), 2.87 (dd, *J* = 3, 6 Hz, H-8′); ^{13}C-NMR (100 MHz, Me_2CO-d_6) δ 37.4 (C-7″), 47.0, 48.9, 50.1, 51.0 (C-2, C-5, C-7′, and C-8′), 72.4 (C-4), 74.0 (C-8″), 115.5 (C-2′), 116.0 (C-5′ and C-5″), 117.3 (C-2″), 117.8 (C-8), 119.9 (C-6′), 121.7 (C-6″), 129.0 (C-1″), 136.3, 136.7 (C-6 and C-1′), 142.0, 143.4, 144.9, 145.7, 145.8 (C-7, C-3′, C-4′, C-3″ and C-4″), 166.6 (C-9), 171.0 (C-9″), 175.6 (C-9′), 207.9 (C-3); CD (8.1 × 10^{-5} M, EtOH) $\Delta\epsilon_{294}$ 11.3, $\Delta\epsilon_{251}$ 0, $\Delta\epsilon_{228}$ −5.5.

Yunnaneic acid C (6): yellow amorphous powder, $[\alpha]^{25}_D$ +106.9° (*c* 0.5, MeOH); UV-vis (EtOH) λ max (log ϵ) 277 (4.3), 230 sh (4.2); IR (KBr) 3410, 1735, 1720, 1700, 1685, 1625 cm^{-1}; FABMS negative ion (−) *m*/*z* 629 ([M − H + glycerol]), 569 ([M − H + MeOH]), 537 ([M − H]); ^{1}H NMR (400 MHz, Me_2CO-d_6) δ 7.47 (d, *J* = 15.8 Hz, 1H, H-7), 6.84 (br s, 1H), 6.82 (d, *J* = 1.8 Hz, 1H, H-2″), 6.75 (d, *J* = 8.0 Hz, 1H, H-5″), 6.69 (br s, 1H), 6.66 (dd, *J* = 1.8, 8.0 Hz, 1H, H-6″), 6.52 (br s, 1H), 6.42 (d, *J* = 15.8 Hz, 1H, H-8), 5.26 (dd, *J* = 4.0, 8.4 Hz, 1H, H-8″), 4.32 (dd, *J* = 1.8, 4.0 Hz, 1H, H-5), 3.79 (t, *J* = 2.9 Hz, 1H, H-2), 3.74 (dd, *J* = 2.9, 7.0 Hz, 1H, H-8′), 3.31 (br s, 1H, H-7′), 3.14 (dd, *J* = 4.0, 14.3 Hz, H-7″), 3.03 (dd, *J* = 8.4, 14.3 Hz, 1H, H-7″); ^{13}C NMR (100 MHz, Me_2CO-d_6) δ 37.3 (C-7″), 74.1 (C-8″), 115.8, 116.0, 117.2 (C-2′, C-5′, C-2″, and C-5″), 119.9 (C-8), 120.0, 121.6 (C-6′ and C-6″), 128.9 (C-1″), 144.8, 145.7 (C-3″ and C-4″), 166.3 (C-9), 170.9 (C-9″), 174.4 (C-9′); CD (9.7 × 10^{-5} M, EtOH) $\Delta\epsilon_{355}$ 0, $\Delta\epsilon_{335}$ −4.2, $\Delta\epsilon_{306}$ 0, $\Delta\epsilon_{279}$ 14.8, $\Delta\epsilon_{238}$ 0, $\Delta\epsilon_{222}$ −7.1.

Preparation of Quinoxaline Derivative 6a. To a solution of **6** (150 mg) in 20% HOAc in EtOH (10 mL) was added *o*-phenylenediamine (60 mg). The solution was stirred for 3 h at 60 °C. The product was purified by Sephadex LH-20 (2.0 cm i.d. × 25 cm) with 80% MeOH to give 95 mg of **6a**: brown amorphous powder; $[\alpha]^{25}_D$ +75.1° (*c* 0.4, MeOH); UV-vis (EtOH) λ max (log ϵ) 318 (4.1), 281 (4.4), 238 (4.6); FABMS negative ion (−) *m*/*z* 609 ([M − H]); ^{1}H NMR (500 MHz, Me_2CO-d_6) δ 8.04 (m, 2H, H-3‴ and 4‴), 7.79 (m, 2H, H-2‴ and 5‴), 7.53 (d, *J* = 15.8 Hz, 1H, H-7), 7.22 (br d, *J* = 6.2 Hz, 1H, H-6), 6.81 (d, *J* = 2.1 Hz, 1H, H-2″), 6.84 (d, *J* = 2.1 Hz, 1H, H-2′), 6.81 (d, *J* = 8.0 Hz, 1H, H-5″), 6.75 (d, *J* = 8.0 Hz, 1H, H-5′), 6.67 (dd, *J* = 2.1, 8.0 Hz, 1H, H-6″), 6.64 (dd, *J* = 2.1, 8.0 Hz, 1H, H-6′), 6.56 (d, *J* = 15.8 Hz, 1H, H-8), 5.21 (dd, *J* = 3.9, 8.7 Hz, 1H, H-8″), 4.95 (t, *J* = 2.1 Hz, 1H, H-2), 4.39 (dd, *J* = 2.0, 6.2 Hz, 1H, H-5), 3.61 (dd, *J* = 2.0, 6.2 Hz, 1H, H-7′), 3.17 (dd, *J* = 2.1, 6.2 Hz, 1H, H-8′), 3.13 (dd, *J* = 3.9, 14.2 Hz, 1H, H-7″), 3.02 (dd, *J* = 8.7, 14.2 Hz, 1H, H-7″); ^{13}C-NMR (100 MHz, Me_2CO-d_6) δ 37.3 (C-7″), 46.4 (C-2), 48.2 (C-7′), 51.1 (C-5), 51.8 (C-8′), 74.2 (C-8″), 115.5 (C-2′), 115.9 (C-5″), 116.2 (C-5′), 117.3 (C-2″), 118.3 (C-8), 119.7 (C-6′), 121.4 (C-6″), 128.8 (C-1″), 129.47, 129.50 (C-3‴ and C-4‴), 130.3, 130.1 (C-2‴ and C-5‴), 134.5 (C-1′), 141.2, 141.3 (2C) (C-7, C-1‴ and C-6‴), 141.5 (C-6), 144.5 (C-1), 144.8, 145.1 (C-4′ and C-4″), 145.6, 146.00 (C-3′ and C-3″), 155.3 (C-3), 157.8 (C-4), 166.6 (C-9), 171.3 (C-9″), 173.9 (C-9′); CD (1.8 × 10^{-5} M, EtOH) $\Delta\epsilon_{344}$ 0, $\Delta\epsilon_{321}$ −4.9, $\Delta\epsilon_{310}$ 0, $\Delta\epsilon_{288}$ 16.3, $\Delta\epsilon_{250}$ 11.5, $\Delta\epsilon_{243}$ 20.2, $\Delta\epsilon_{236}$ 0, $\Delta\epsilon_{226}$ −29.2.

Preparation of *p*-Dimethoxyphenylamino Derivatives 5a and 5b. To a solution of **5** (70 mg) in 10% HOAc in EtOH (2 mL) was added *p*-anisidine (100 mg). The mixture was stirred for 3.5 h at room temperature and then treated with excess $NaBH_3CN$. The mixture was separated by Sephadex LH-20 column with 60% MeOH and then MCI−gel CHP 20P chromatography with 50−70% MeOH to give **5b** (10.4 mg) and **5a** (6.7 mg).

Compoubd 5a: tan amorphous powder, $[\alpha]^{19}_D$ +113.5° (*c* 0.3, MeOH); UV-vis (EtOH) λ max (log ϵ) 264 (4.2); FABMS negative ion (−) *m*/*z* 628 ([M − H]); ^{1}H NMR (500 MHz, pyridine-d_5) δ 7.67 (2H, d, *J* = 9.2 Hz, H-2‴, 6‴), 7.45 (1H, d, *J* = 15.7 Hz, H-7), 6.97 (2H, d, *J* = 9.2 Hz, H-3‴, 5‴), 6.83 (1H, d, *J* = 2.1 Hz, H-2″), 6.74 (1H, d, *J* = 8.0 Hz, H-5″), 6.70 (1H, br d, *J* = 6.6 Hz, H-6), 6.64 (1H, dd, *J* = 2.1, 8.0 Hz, H-6″), 6.61 (1H, d, *J* = 2.1 Hz, H-2′), 6.40 (1H, dd, *J* = 2.1, 8.0 Hz, H-6′), 6.31 (1H, d, *J* = 15.7 Hz, H-8), 5.20 (1H, dd, *J* = 3.9, 8.9 Hz, H-8″), 4.06 (1H, d, *J* = 3.7 Hz, H-4), 4.03 (1H, br t, *J* = 4 Hz, H-2), 3.81 (3H, s, OCH_3), 3.78 (1H, dd, *J* = 1.4, 5 Hz, H-3), 3.40 (1H, m, H-5), 3.20 (1H, br s, H-7′), 3.11 (1H, dd, *J* = 3.9, 14.4 Hz, H-7″), 2.99 (1H, dd, *J* = 8.9, 14.4 Hz, H-7″), 2.64 (1H, m, H-8′); ^{13}C NMR (50 MHz, Me_2CO-d_6) δ 37.3 (C-7″), 38.0, 45.8, 48.8, 49.5 (C-2, C-3, C-5, C-7′, and C-8′), 55.6 (OCH_3), 66.2 (C-4), 73.9 (C-8″), 114.7 (2C, C-3‴, 5‴), 115.6, 115.8 (2C) (C-2′, C-5′, and C-5″), 116.4 (C-8), 117.1 (C-2″), 119.8 (C-2′), 121.3 (C-6″), 121.9 (2C, C-2‴, 6‴), 128.8 (C-1″), 133.0 (C-1‴), 135.5, 136.1, 141.7, 144.0 (2C), 144.7, 145.4, 145.6 (C-1, C-6, C-7, C-1′, C-3′, C-4′, C-3″, C-4″), 157.4 (C-4‴), 166.9 (C-9), 171.3 (C-9″), 176.4 (C-9′); CD (3.2 × 10^{-5} M, EtOH) $\Delta\epsilon_{290}$ 7.3, $\Delta\epsilon_{279}$ 0, $\Delta\epsilon_{272}$ −4.8, $\Delta\epsilon_{264}$ 0, $\Delta\epsilon_{250}$ 9.9, $\Delta\epsilon_{230}$ 1.1.

Compound 5b: tan amorphous powder; $[\alpha]^{19}_D$ +72.2° (*c* 0.3, MeOH); UV-vis (EtOH) λ max (log ϵ) 275 (4.2), 251 (4.2); FABMS negative ion (−) *m*/*z* 646 ([M − H]);

^{1}H NMR (400 MHz, Me_2CO-d_6) Table 2; ^{1}H NMR (300 MHz, pyridine-d_5) δ 7.45 (1H, d, J = 16 Hz, H-7), 6.80 (overlapped, H-6), 6.80 (1H, d, J = 2 Hz, H-2″), 6.77 (1H, d, J = 2 Hz, H-2′), 6.64−6.75 (m), 6.59 (1H, dd, J = 2, 8 Hz, H-6″), 6.52 (1H, dd, J = 2, 8 Hz, H-6′), 5.83 (1H, d, J = 16 Hz, H-8), 5.51 (1H, dd, J = 5, 9 Hz, H-8″), 4.36 (1H, dd, J = 3, 8 Hz, H-4), 3.89 (1H, dd, J = 2, 8 Hz, H-3), 3.70 (3H, s, OCH_3), 3.69 (1H, br s, H-2), 3.37 (1H, br d, J = 7 Hz, H-7′), 3.11 (1H, m, H-5), 3.07 (1H, dd, J = 5, 14 Hz, H-7″), 2.96 (1H, dd, J = 9, 14 Hz, H-7″), 2.47 (1H, dd, J = 2, 7 Hz, H-8′); ^{13}C NMR (50 MHz, Me_2CO-d_6) δ 37.3 (C-7″), 38.7, 43.2, 48.0, 51.6, 53.2 (C-2, C-3, C-5, C-7′, and C-8′), 55.8 (OCH_3), 71.1 (C-4), 73.9 (C-8″), 115.1 (2C), 115.2 (C-2′, C-5′, and C-5″), 115.6 (2C), 115.9 (2C) (C-2‴, C-3‴, C-5‴, and C-6‴), 116.1 (C-8), 117.1 (C-2″), 119.2 (C-2′), 121.4 (C-6″), 128.9 (C-1″), 137.4, 141.4, 141.5, 142.9 (C-6, C-7, C-1′ and C-1‴), 144.3, 144.4, 145.4, 145.6 (C-3′, C-4′, C-3″, and C-4″), 152.7 (C-4‴), 166.9 (C-9), 171.4 (C-9″), 175.3 (C-9′); CD (2.0×10^{-5} M, EtOH) $\Delta\epsilon_{289}$ 19.3, $\Delta\epsilon_{270}$ 3.7, $\Delta\epsilon_{265}$ 3.9, $\Delta\epsilon_{254}$ 0, $\Delta\epsilon_{230}$ −7.6.

Preparation of bis-*p*-Dimethoxyphenylamino Derivative 6b. To a solution of **6** (100 mg) in 10% HOAc in EtOH (5 mL) was added *p*-anisidine (800 mg). The solution was stirred for 1 h at 80 °C. To the mixture excess of $NaBH_3CN$ was added at 80 °C and stirred for 12 h at room temperature. The mixture was separated by Sephadex LH-20 and then Chromatorex ODS chromatography with aqueous MeOH to yield **6b** (23 mg) as tan amorphous powder, $[\alpha]^{25}_D$ −12.6° (*c* 0.3, MeOH); UV-vis (EtOH) λ max (log ϵ) 255 (4.6); FABMS negative ion (−) *m*/*z* 733 ([M − H]); ^{1}H NMR (300 MHz, Me_2-CO-d_6) δ 7.69 (d, J = 9 Hz, 2H, H-2‴, 6‴), 7.44 (d, J = 16 Hz, 1H, H-7), 6.87 (br d, J = 7 Hz, 1H, H-6), 6.83 (d, J = 9 Hz, 2H, H-3‴, 5‴), 6.83 (d, J = 2 Hz, 1H, H-2″), 6.75 (d, J = 8 Hz, 1H, H-5″), 6.66 (m, 6H, H-5′, 6″ and H-2⁗, 3⁗, 5⁗, 6⁗), 6.55 (d, J = 2 Hz, 1H, H-2′), 6.38 (dd, J = 2, 8 Hz, 1H, H-6′), 6.56 (d, J = 6 Hz, 1H, H-8), 5.23 (dd, J = 4, 9 Hz, 1H, H-8″), 4.41 (ddd, J = 1, 6, 7.5 Hz, 1H, H-3), 4.13 (ddd, J = 1, 5, 6 Hz, 1H, H-2), 3.70 (br s, 1H, H-7′), 3.56 (br d, J = 7.5 Hz, 1H, H-4), 3.18 (m, 1H, H-5), 3.14 (dd, J = 4, 14 Hz, 1H, H-7″), 3.01 (dd, J = 9, 14 Hz, 1H, H-7″), 2.70 (br s, 1H, H-8′); ^{13}C NMR (100 MHz, Me_2CO-d_6) δ 37.4 (C-7″), 41.0 (C-2), 41.6 (C-7′), 46.0 (C-5), 50.6 (C-8′), 55.5 (C-4), 55.6, 55.8 (OCH_3), 58.1 (C-3), 73.8 (C-8″), 114.3 (2C) (C-2‴ and C-6‴), 115.4 (2C) (C-2⁗ and C-6⁗), 115.6 (2C) (C-3⁗ and C-5⁗), 115.7, 115.8 (C-2′, C-5′), 115.9 (C-5″), 117.0 (C-8), 117.2 (C-2″), 120.0 (C-6′), 121.6 (C-6″), 123.6 (2C) (C-3⁗, 5⁗), 129.0 (C-1″), 134.1 (C-1‴), 136.5 (C-1′), 137.2 (C-1), 142.2 (C-1⁗), 143.9 (C-7), 144.1 (C-6), 144.3 144.6 (C-4′ and C-4″), 145.4, 145.6 (C-3′ and C-3″), 153.1 (C-4⁗), 157.1 (C-4‴), 166.9 (C-9), 171.1 (C-9″), 177.0 (C-9′); CD (6.3×10^{-5} M, EtOH) $\Delta\epsilon_{337}$ −2.5, $\Delta\epsilon_{292}$ 0, $\Delta\epsilon_{271}$ −12.6, $\Delta\epsilon_{258}$ 0, $\Delta\epsilon_{244}$ 23.9, $\Delta\epsilon_{226}$ 0.

Yunnaneic acid B (4): tan amorphous powder, $[\alpha]^{25}_D$ +80.5° (*c* 0.3, MeOH); UV-vis (EtOH) λ max (log ϵ) 277 (4.6), 225 sh (4.5); FABMS negative ion (−) *m*/*z* 1093 ([M − H]); ^{1}H NMR (400 MHz, Me_2CO-d_6) Table 2; ^{1}H NMR (500 MHz, pyridine-d_5) δ 7.81 (d, J = 15.8 Hz, 1H, A-7), 7.50 (d, J = 15.8 Hz, 1H, B-7), 7.49 (d, J = 2.1 Hz, 1H, A-2″), 7.44 (d, J = 2.1 Hz, 1H, B-2″), 7.35 (d, J = 2.1 Hz, 1H, A-2′), 7.28 (d, J = 8.0 Hz, 1H, B-5′), 7.19 (d, J = 8.0 Hz, 1H, B-5″), 7.19 (d, J = 8.0 Hz, 1H, A-5″), 7.16 (d, J = 8.0 Hz, 1H, A-5′), 7.14 (d, J = 2.1 Hz, 1H, B-2′), 7.07 (dd, J = 2.1, 8.0 Hz, 1H, A-6″), 7.03 (dd, J = 2.1, 8.0 Hz, 1H, A-6′), 7.01 (dd, J = 2.1, 8.0 Hz, 1H, B-6″), 6.96 (dd, J = 2.1, 8.0 Hz, 1H, B-6′), 6.76 (br d, J = 6.0 Hz, 1H, A-6), 6.70 (br d, J = 6.2 Hz, 1H, B-6), 6.51 (d, J = 15.8 Hz, 1H, A-8), 6.46 (d, J = 15.8 Hz, 1H, B-8), 6.02 (t, J = 6.0 Hz, 1H, A-8″), 5.89 (dd, J = 4.2, 8.2 Hz, 1H, B-8″), 4.87 (br d, J = 7.3 Hz, 1H, A-7′), 4.50 (br s, 1H, A-2), 4.45 (br d, J = 8.5 Hz, 1H, B-7′), 4.38 (br s, 1H, B-2), 3.59 (m, 3H, A-7″ and B-7″), 3.58 (dd, J = 1.6, 6.0 Hz, 1H, A-5), 3.49 (dd, J = 8.5, 14.5 Hz, 1H, B-7″), 3.40 (dd, J = 2.4, 7.4 Hz, 1H, B-8′), 3.05 (dd, J = 1.7, 6.4 Hz, 1H, B-5), 2.97 (dd, J = 2.3, 7.3 Hz, 1H, A-8′); ^{13}C NMR (100 MHz, Me_2CO-d_6) Table 2; CD (5.1×10^{-5} M, EtOH) $\Delta\epsilon_{295}$ 15.5, $\Delta\epsilon_{278}$ 0, $\Delta\epsilon_{250}$ −0.2, $\Delta\epsilon_{225}$ −5.9, $\Delta\epsilon_{214}$ 0.

(*R*)-3-(3,4-Dihydroxyphenyl)lactic Acid from 4. A solution of **4** (100 mg) in 0.25 M H_2SO_4 (5 mL) was heated at 90 °C for 5 h. The mixture was applied to a column of MCI−gel CHP 20P with H_2O to give (*R*)-3-(3,4-dihydroxyphenyl)lactic acid (17 mg) along with the unreacted of **4** (22 mg).

Treatment of 4 with *o*-Phenylenediamine. To a solution of **3** (150 mg) in 20% HOAc in EtOH (10 mL) was added *o*-phenylenediamine (80 mg). The solution was stirred for 4 h at 70 °C. The product was separated by Sephadex LH-20 chromatography with aqueous MeOH (80%) to afford **6b** (23 mg).

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References and Notes

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