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Components of *Broussonetia kazinoki* SIEB. I. Structures of Two New Isoprenylated Flavans and Five New Isoprenylated 1,3-Diphenylpropane Derivatives[1,2]

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Two new isoprenylated flavans, kazinols E and H, and five new isoprenylated 1,3-diphenylpropane derivatives, kazinols C, D, F, G, and K, were isolated from the extract of the root bark of *Broussonetia kazinoki* SIEB. (Japanese name, Himekōzo, Moraceae). On the basis of chemical and spectral evidence, the structures of kazinols E and H were shown to be **3** and **6**, respectively, and the structures of kazinols C, D, F, G, and K to be **1**, **2**, **4**, **5**, and **7**, respectively.

Keywords——*Broussonetia kazinoki*; Moraceae; flavan; 1,3-diphenylpropane; ^{1}H-NMR; ^{13}C-NMR; nuclear Overhauser effect

Previously we reported the structure determination of a series of natural Diels–Alder type adducts as well as isoprenylated flavonoids isolated from the root bark of cultivated mulberry tree and the Chinese crude drug "Sang-Bai-Pi" (Japanense name "Sōhakuhi"), the latter imported from the People's Republic of China.[3] Furthermore we reported the phenolic components of *Cudrania tricuspidata* (CARR.) BUR.[4] and *Broussonetia papyrifera* (L.) VENT.,[2,5] both of which belong to the family Moraceae. In the course of our studies on the phenolic constituents of Moraceae plants, we studied the root bark of *Broussonetia kazinoki* SIEB. (Japanese name "Himekōzo"), which is a deciduous tree distributed over Korea, China, Taiwan, and Japan. Its cortex has been used as a raw material for paper and also as a Chinese crude drug, as has the cortex of *B. papyrifera* (L.) VENT. (Japanese name "kazinoki").[6] In this paper, we report the structure determination of two isoprenylated flavans, kazinols E and H, and of five isoprenylated 1,3-diphenylpropane derivatives, kazinols C, D, F, G, and K, obtained from the root bark of *B. kazinoki* SIEB.

The dried root bark of *B. kazinoki* SIEB. was extracted successively with *n*-hexane and benzene. The *n*-hexane extract was fractionated sequentially by column chromatography and preparative thin-layer chromatography (TLC) to give kazinols C (**1**), D (**2**), E (**3**), G (**5**), H (**6**), and K (**7**). A part of the benzene extract was also fractionated sequentially by preparative TLC to give kazinol F (**4**).

Kazinol C (**1**) was obtained as an oily substance, $M^+ = 464.2924$, $C_{30}H_{40}O_4$, exhibiting a positive ferric chloride test and sodium molybdate test.[7] The infrared (IR) spectrum of **1** suggested the presence of hydroxyl groups [3650 (sh), 3600 (sh), 3530 (br) cm^{-1}] and aromatic rings [1625, 1600 (sh) cm^{-1}]. Treatment of **1** with dimethyl sulfate and potassium carbonate in acetone gave a tetramethyl ether (**1a**). Acetylation of **1** with acetic anhydride in pyridine gave a triacetate (**1b**) and a tetraacetate (**1c**). The ultraviolet (UV) spectrum of **1** showed absorption maxima at 218 (log $\varepsilon = 4.59$) and 286 nm (3.97), which indicated the presence of an unconjugated aromatic system.[2,8] The proton nuclear magnetic resonance (^{1}H-NMR)

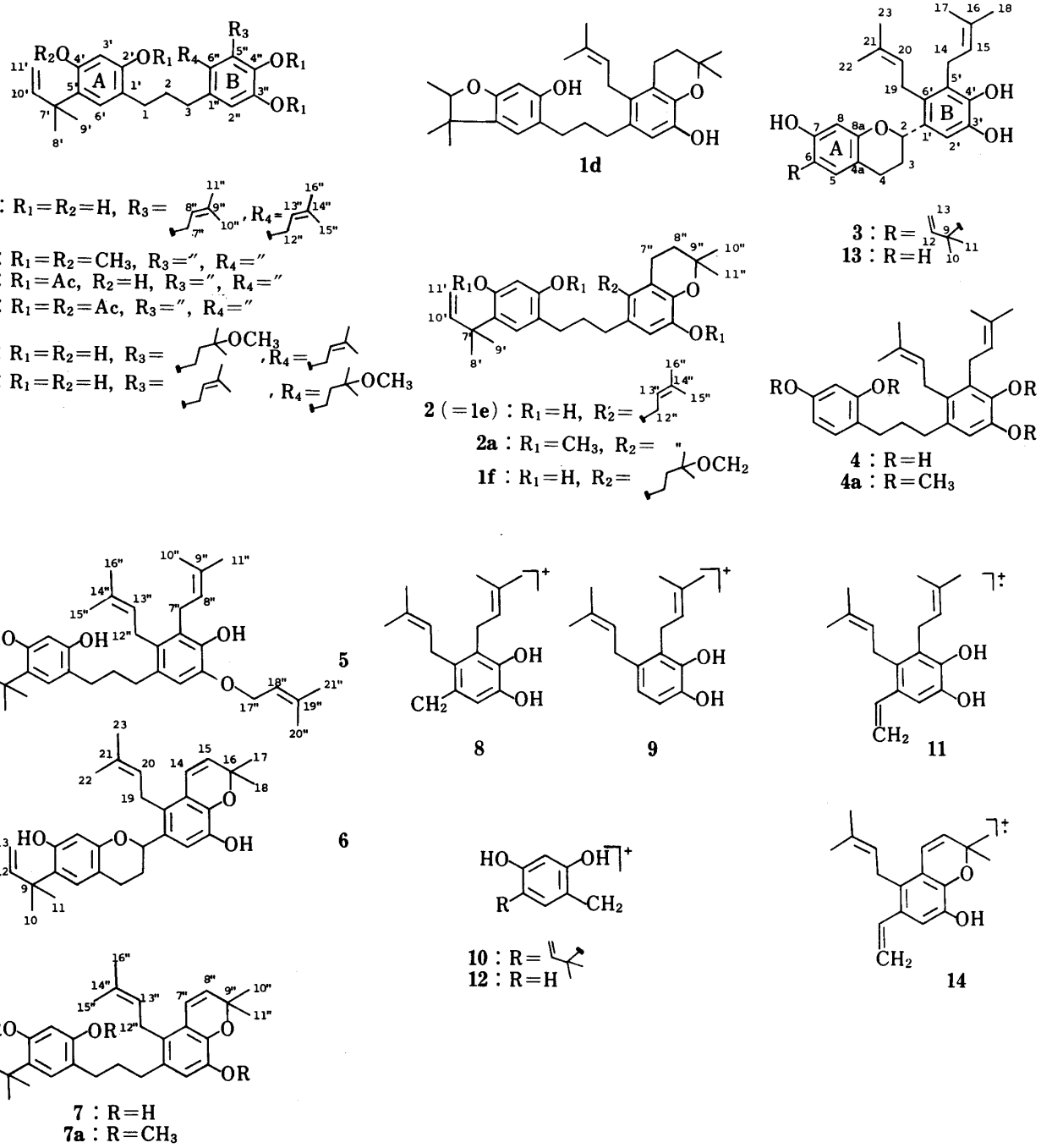

Fig. 1

spectrum of **1** indicated the presence of two 3,3-dimethylallyl groups, a 1,1-dimethylallyl group, and three aromatic protons: δ 1.66, 1.70, 1.72, 1.78 (each 3H, s), 3.23 (2H, d, $J=7$ Hz), 3.34 (2H, d, $J=7$ Hz), 4.96 (1H, t, $J=7$ Hz), 5.12 (1H, t, $J=7$ Hz); δ 1.38 (6H, s), 5.25 (1H, d, $J=10$ Hz), 5.31 (1H, d, $J=18$ Hz), 6.16 (1H, dd, $J=10$ and 18 Hz); δ 6.30 (1H, s), 6.61 (1H, s), 6.93 (1H, s). The ^{1}H-NMR spectrum also indicated the presence of a 1,3-disubstituted propane moiety: δ 1.82 (2H, quintet, $J=7$ Hz), 2.55 (2H, t, $J=7$ Hz), 2.59 (2H, t, $J=7$ Hz). The mass spectrum (MS) of **1** showed significant fragments[9] at m/z 408 ($M^+ - C_4H_8$), 396 ($M^+ - C_5H_8$), 340 ($396 - C_4H_8$), 273 ($M^+ - 191$), 259 (**8**), 245 (**9**), 205 ($M^+ - 259$), 203 ($259 - C_4H_8$), 191 (**10**), 123 ($191 - C_5H_8$). From the above results, it was suggested that kazinol C is a 1,3-diphenylpropane derivative having two isoprenyl groups and two hydroxyl groups in one of the phenyl moieties, and an isoprenyl group and two hydroxyl groups in the other

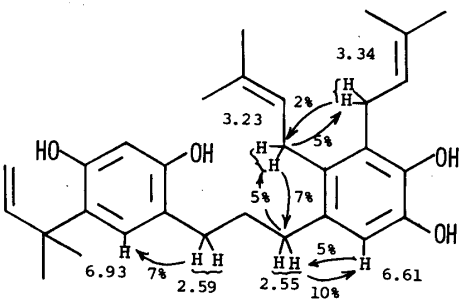

Fig. 2. NOE Results for Kazinol C ($CDCl_3$)
%: Increase of signal area.

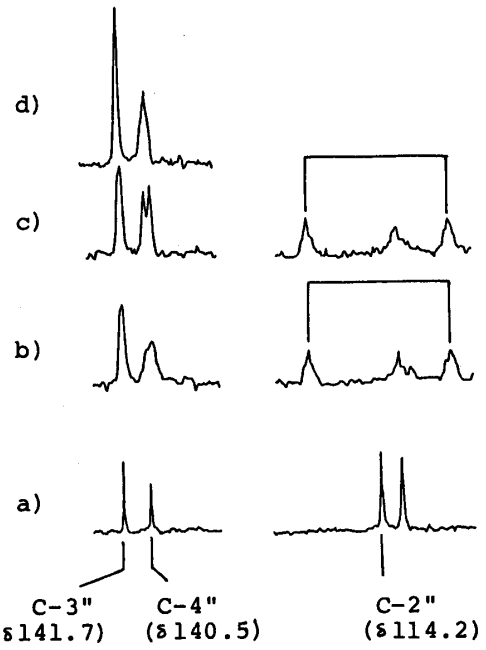

Fig. 3. LSPD Measurement of Kazinol C
a) ^{13}C-{^1H} Complete decoupling.
b) ^{13}C-{^1H} Non-decoupling.
c) Irradiated at δ 3.3 ($C_{7''}$-H × 2 and $C_{12''}$-H × 2).
d) Irradiated at δ 6.61 ($C_{2''}$-H).

phenyl moiety. In the carbon-13 nuclear magentic resonance (^{13}C-NMR) studies, the carbon atoms of **1** were assigned by the off-resonance decoupling technique as well as by comparing the ^{13}C-NMR spectrum of **1** with those of model compounds[2,10] and by the long-range selective ^1H decoupling (LSPD) technique (Table I). In the ^{13}C-NMR spectrum of **1**, the chemical shift values of the carbon atoms at the C-3″ and -4″ positions were similar to those of the corresponding carbon atoms of 3′,4′-dioxygenated flavonoids.[2,11] Based on the biogenetic analogy to the 1,3-diphenylpropane derivatives obtained from the plants of *Broussonetia* species and the spectral data (MS and ^1H-NMR),[2,12] the A ring of **1** seems to be a 2′,4′-dihydroxy-5′-isoprenylated phenyl moiety. The substitution pattern of the A and B rings was also supported by the nuclear Overhauser effects (NOE), which were observed as follows: (1) at the C-3 protons (δ 2.55) when the aromatic proton at C-2″ (δ 6.61) was irradiated, (2) at the C-12″ protons (δ 3.23) and the C-2″ proton when the C-3 protons were irradiated, (3) between the protons at C-12″ and those at the C-7″ (δ 3.34) and C-3 positions when the C-12″ protons (δ 3.23) were irradiated, (4) between the protons at C-7″ and those at C-12″ when the C-7″ protons (δ 3.34) were irradiated, and (5) between the C-1 protons (δ 2.59) and the C-6′ proton (δ 6.93) when the C-1 protons (δ 2.59) were irradiated (Fig. 2). These results suggest that the B ring is a 3″,4″-dihydroxy-5″,6″-bis(3,3-dimethylallyl)phenyl moiety and that the A ring is a 2′,4′-dihydroxy-5′-(1,1-dimethylallyl)phenyl moiety. The substitution pattern of the B ring was further supported by the result of the LSPD technique and the chemical shift values of methoxyl carbons of the tetramethyl ether (**1a**). The LSPD technique yielded the following observations. When the C-2″ proton (δ 6.61) was weakly irradiated, the signals of the C-3″ (δ 141.7) and C-4″ (δ 140.5) carbon atoms changed. When the C-12″ (δ 3.23) and C-7″ (δ 3.34) protons were weakly irradiated, the C-4″ carbon signal changed, while the C-2″ (δ 114.2) and C-3″ carbon signals showed no change (Fig. 3). On the other hand, it was reported that the signal of the di-*ortho*-substituted methoxyl carbon nucleus appears at δ *ca.* 60 ppm, while that of the mono-*ortho*-substituted methoxyl carbon nucleus appears at *ca.* 55 ppm.[13] In the case of **1a**, the signals of

TABLE I. ^{13}C-NMR Chemical Shifts (ppm) **1**—**7**

	1	**2**	**4**	**5**	**7**		**3**	**6**
C-1	32.9[a]	32.7[a]	33.6[a]	33.1[a]	32.6[a]	C-2	75.0	74.8
C-2	29.7	29.7	30.4	29.7	29.5	C-3	25.6	25.7
C-3	31.6[a]	31.7[a]	33.1[a]	31.8[a]	31.4[a]	C-4	29.9	29.8
C-1′	120.7	120.5	120.5	120.0	119.5	C-4a	113.9	113.3
C-2′	153.2	153.7[b]	157.3[b]	153.6[b]	152.8[b]	C-5	127.0	127.0
C-3′	105.0	104.8	103.4	104.9	104.3	C-6	125.1	124.9
C-4′	153.2	153.3[b]	156.6[b]	153.1[b]	152.6[b]	C-7	153.5[a]	153.9[a]
C-5′	124.4	124.0	107.3	124.5	123.7	C-8	105.6	105.8
C-6′	127.7	127.6	131.1	127.6	127.0	C-8a	155.1[a]	155.4[a]
C-1″	133.0	132.0	132.7	131.2	132.3	C-1′	131.0	131.3
C-2″	114.2	113.1	114.6	111.1	115.0	C-2′	111.3	112.9
C-3″	141.7	143.0	143.0	143.7	141.9	C-3′	142.4	143.3
C-4″	140.5	139.2	142.2	142.2	137.0	C-4′	141.7	139.3
C-5″	130.5	119.8	130.4	130.7	119.2	C-5′	130.2	119.8
C-6″	127.0	128.9	127.7	126.5	126.2	C-6′	127.0	126.4
C-7′	39.8	39.8		39.8	39.6	C-9	39.8	39.9
C-8′	27.3	27.3		27.3	27.1	C-10	27.2	27.4
C-9′	27.3	27.3		27.3	27.1	C-11	27.2	27.4
C-10′	148.5	148.6		148.3	147.8	C-12	148.3	148.5
C-11′	113.1	112.7		113.1	112.5	C-13	113.0	113.8
C-7″	27.8[b]	20.3	28.1[c]	27.7[c]	119.6	C-14	27.2[b]	120.0
C-8″	122.7[c]	33.2	124.9[d]	123.3[d]	129.8	C-15	122.8[c]	130.8
C-9″	133.3[d]	74.0	130.7[e]	131.5[e]	75.5	C-16	132.4[d]	76.3
C-10″	18.0	26.6	18.0	17.9[f]	27.5	C-17	17.9	27.7
C-11″	25.7	26.6	25.8	25.7	27.5	C-18	25.6	28.1
C-12″	26.1[b]	27.3	26.2[c]	25.6[c]	26.7	C-19	25.6[b]	26.5
C-13″	124.4[c]	123.6	125.8[d]	124.4[d]	123.6	C-20	124.1[c]	123.9
C-14″	130.9[d]	131.0	130.7[e]	131.2[e]	130.2	C-21	131.4[d]	132.2
C-15″	18.0	17.9	18.0	18.0[f]	17.9	C-22	17.9	18.2
C-16″	25.7	25.7	25.8	25.7	25.5	C-23	25.6	25.7
Solv.	A	A	B	A	A		A	A

Solvent: A, $CDCl_3$; B, acetone-d_6. *a*—*f*) Assignments may be interchanged in each column.

TABLE II. Acetylation Shifts for $C_{3'}$-, $C_{6'}$-, $C_{10'}$-, $C_{11'}$- and $C_{2''}$-H of **1b** and **1c**

	$C_{3'}$-H	$C_{6'}$-H	$C_{10'}$-H	$C_{11'}$-H		$C_{2''}$-H
1b	6.50	7.10	6.20	5.33	5.38	6.90
1c	6.79	7.26	5.99	5.00	5.03	6.91
Δ	−0.23	−0.16	+0.21	+0.33	+0.35	−0.01

Measured in $CDCl_3$ (ppm).

methoxyl carbons appeared at δ 55.4 (×2), 55.7, and 60.6 ppm. This results suggests that one of the methoxyl groups is di-*ortho*-substituted. The substitution pattern of the A ring was further supported by observation of the acetylation shift of the A ring proton signals of **1b** and **1c**. Comparison of the ^{1}H-NMR spectra of **1**, **1b**, and **1c** indicates that the acetylation of the hydroxyl group of **1b** caused a remarkable downfield shift of the proton at C-3′ position and an upperfield shift of the protons at C-10′ and -11′ (Table II). This result suggests that the 1,1-dimethylallyl group is located at the C-5′ position. From the above results, the formula **1** was suggested for the structure of kazinol C.

The formula (**1**) was further supported by the following results. A mixture of **1** and hydrochloric acid in methanol was kept at 60 °C for 2 h. The reaction mixture was purified by preparative TLC to give **1d**, **1e**, **1f**, and **1g**. Compound **1e** was identical with kazinol D, and the structures of the reaction products were supported by the spectral data. The MS of **1d** gave the MS which showed the molecular ion peak at *m/z* 464. The ^{1}H-NMR spectrum of **1d** indicated the presence of a 3,3-dimethylallyl group and a 2,2-dimethyldihydropyran ring system, δ 1.70 (6H, s), 3.17 (2H, d, J=7 Hz), 4.92 (1H, t, J=7 Hz); δ 1.32 (6H, s), 1.80 (2H, t, J=7 Hz), 2.45—2.75 (2H, m), as well as a 1,3-diphenylpropane moiety, δ 1.60—1.90 (2H, m), 2.58 (2H, t, J=7 Hz), 2.64 (2H, t, J=7 Hz). The presence of a 2-methyl-3,3-dimethyl-5,6-disubstituted dihydrobenzofuran moiety[14] and an aromatic proton was indicated: δ 1.25 (3H, s), 1.38 (3H, d, J=7 Hz), 1.66 (3H, s), 4.30 (1H, q, J=7 Hz), 6.21 (1H, s), 6.75 (1H, s); δ 6.62 (1H, s). From the above results, the structure (**1d**) was suggested. The MS of **1f** showed the molecular ion peak at *m/z* 496. The ^{1}H-NMR of **1f** showed the presence of a 1,1-dimethylallyl group, a 2,2-dimethyldihydropyran ring system, and a 3-methyl-3-methoxybutyl moiety: δ 1.42 (6H, s), 5.26 (1H, d, J=10 Hz), 5.29 (1H, d, J=18 Hz), 6.16 (1H, dd, J=10 and 18 Hz); δ 1.34 (6H, s), 1.82 (2H, t, J=7 Hz), 2.30—2.80 (8H, m, overlapping the signals of the protons at C-1, -3, -7″, and -12″); δ 1.23 (6H, s), 1.50—1.95 (4H, m, overlapping the signals of protons at C-2 and -13″), 3.26 (3H, s). From the above results, the structure **1f** was suggested. The MS of **1g** showed the molecular ion peak at *m/z* 496. The ^{1}H-NMR spectrum indicated the presence of a 3,3-dimethylallyl group, a 1,1-dimethylallyl group, and a 3-methyl-3-methoxybutyl moiety: δ 1.67, 1.72 (each 3H, s), 3.21 (2H, d, J=7 Hz), 4.96 (1H, t, J=7 Hz); δ 1.39 (6H, s). 5.24 (1H, d, J=10 Hz), 5.29 (1H, d, J=18 Hz), 6.15 (1H, dd, J=10 and 18 Hz); δ 1.20 (6H, s), 1.60—1.90 (4H, m, overlapping the signals of protons at C-2 and -8″ (or -13″)), 2.40—2.80 (6H, m, overlapping the signals of protons at C-1, -3, and -7″ (or -12″)), 3.28 (3H, s). From these results, two possible structures (**1g** and **1g′**) were suggested. Comparison of the chemical shift values of the 3,3-dimethylallyl group of **1g** and the values of the relevant groups of **1**, **1d**, and **2** (**1e**) indicated that the sturucture **1g** seemed more probable than **1g′**. The ^{1}H-NMR and IR spectra of the flavan compound **3**, which was obtained by treatment of **1** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), were identical with those of kazinol E (**3**). All these results indicate that the structure of kazinol C is represented by formula **1**.

Kazinol D (**2**) was obtained as an oily substance, M^+=464.2927, $C_{30}H_{40}O_4$, exhibiting a positive ferric chloride test, but a negative sodium molybdate test.[7] The IR spectrum of **2** suggested the presence of hydroxyl groups [3615, 3570, 3500 cm^{-1}] and aromatic rings [1625, 1600 cm^{-1}]. Treatment of **2** with dimethyl sulfate and potassium carbonate in acetone gave a trimethyl ether (**2a**). The UV spectrum of **2** showed absorption maxima at 221 (4.67), 230 (infl. 4.07), and 283 nm (3.91). As described in the experimental section, the ^{1}H-NMR spectrum of **2** indicated the presence of a 3,3-dimethylallyl group, a 1,1-dimethylallyl group, and a 2,2-dimethyldihydropyran ring system. The spectrum also indicated the presence of three aromatic protons: δ 6.28 (1H, s), 6.63 (1H, s), 6.91 (1H, s). The MS of **2** showed significant fragments at *m/z* 259, 245, and 191 (**10**),[9] and the spectrum was similar to that of **1**. These results indicated that kazinol D is a 1,3-diphenylpropane derivative having a 3,3-dimethylallyl group, a 1,1-dimethylallyl group, and a 2,2-dimethyldihydropyran ring system. In the ^{13}C-NMR spectrum of **2**, the chemical shift values of the carbon atoms of the 1,3-diphenylpropane skeleton as well as of a 3,3-dimethylallyl group and a 1,1-dimethylallyl group were similar to those of the relevant carbon atoms of **1** except that of the carbon atom at C-5″. In the ^{13}C-NMR spectrum of **2a**, the signals of the methoxyl carbon atoms appeared at δ 55.4 (×2) and 56.0 ppm. This result suggests that all the methoxyl groups of **2a** are mono-*ortho*-substituted.[13] Kazinol D was derived from kazinol C by treatment with hydrochloric acid solution. All these results indicated that the structure of kazinol D is represented by formula **2**.

Kazinol E (**3**) was obtained as colorless needles, mp 147 °C, M^+=462.2803, $C_{30}H_{38}O_4$,

$[\alpha]_D^{18}$ +0.30°, exhibiting a positive ferric chloride test and sodium molybdate test.[7] The IR spectrum of **3** indicated the presence of hydroxyl groups [3590 (sh), 3550, 3490 cm^{-1}] and aromatic rings [1625, 1585 cm^{-1}]. The UV spectrum showed absorption maxima at 224 (4.92), 232 (infl. 4.36), and 288 nm (3.91).[8] As described in the experimental section, the ^{1}H-NMR spectrum of **3** showed the presence of two 3,3-dimethylallyl groups and a 1,1-dimethylallyl group. The spectrum also showed five aliphatic proton signals and three aromatic proton signals: δ 1.70—2.10 (2H, m), 2.62—2.88 (2H, m), 4.80—5.10 (1H, m); δ 6.31 (1H, s), 6.73 (1H, s), 6.83 (1H, s). The MS of **3** showed significant fragments at *m/z* 272 (**11**) and 191 (**10**).[15] In the ^{13}C-NMR spectrum of **3**, the carbon atoms were assigned by the off-resonance decoupling technique as well as by comparing the ^{13}C-NMR spectrum of **3** with those of model compounds (**1**, **2**, kazinols A[2] and B[2]) (Table I). (±)-Kazinol E was derived from **1** by treatment with DDQ. On the basis of the circular dichroism (CD) spectrum, **3** was concluded to have the (*S*)-configuration at the C-2 position.[16] From the above results, kazinol E is represented by the formula **3**.

Kazinol F (**4**) was obtained as colorless needles, mp 108—109 °C, $M^+ = 396.2301$, $C_{25}H_{32}O_4$, exhibiting a positive ferric chloride test, sodium molybdate test,[7] and Gibbs test. The IR spectrum of **4** suggested the presence of hydroxyl groups and aromatic rings. Treatment of **4** with dimethyl sulfate and potassium carbonate in acetone gave a tetramethyl ether (**4a**). The UV spectrum showed absorption maxima at 282 (3.91), 286 nm (sh 3.89). As described in the experimental section, the ^{1}H-NMR spectrum of **4** indicated the presence of two 3,3-dimethylallyl groups and a 1,3-diphenylpropane moiety. The ^{1}H-NMR spectrum also indicated the presence of ABC-type aromatic protons, and an aromatic proton: δ 6.28 (1H, dd, J=2 and 8 Hz), 6.39 (1H, d, J=2 Hz), 6.88 (1H, d, J=8 Hz); δ 6.57 (1H, s). The MS of **4** showed significant fragments[9] at *m/z* 259 (**8**), 245 (**9**), and 123 (**12**). In the ^{13}C-NMR spectrum of **4**, the chemical shift values of the carbon atoms of the 1,3-diphenylpropane skeleton as well as of two 3,3-dimethylallyl groups were similar to those of the relevant carbon atoms of **1** except those of the carbon atoms at C-2′, -4′, -5′, and -6′ (Table I). In the ^{13}C-NMR spectrum of **4a**, the signals of the methoxyl carbon atoms appeared at δ 55.0, 55.1, 55.5, and 60.3 ppm, suggesting that one of the four methoxyl groups is di-*ortho*-substituted.[13] The substitution pattern of the B ring of **4** was supported by the NOE: (1) at the C-3 protons (δ 2.47) when the aromatic proton at C-2″ (δ 6.58) was irradiated, (2) between the protons at C-12″ and those at C-13″ (δ 4.96), C-3 and C-7″ when C-12″ protons (δ 3.21) were irradiated, and (3) between the protons at C-7″ and those at C-12″, C-13″ and C-8″ (δ 5.09) when the C-7″ protons (δ 3.34) were irradiated (Fig. 4). These results suggest that the B ring is a 3″,4″-dihydroxy-5″,6″-bis(3,3-dimethylallyl)phenyl moiety. When kazinol F was treated with DDQ in dry ether, a flavan derivative (**13**) was obtained, the ^{1}H-NMR and IR spectra of which were identical with those of kazinol I isolated from *Broussonetia papyrifera* (L.) VENT.[17] From the above results, kazinol F is represented by fomula **4**.

Kazinol G (**5**) was obtained as an oily substance, $M^+ = 532.3536$, $C_{35}H_{48}O_4$, exhibiting a positive ferric chloride test, but a negative sodium molybdate test.[7] The IR spectrum of **5** suggested the presence of hydroxyl groups and aromatic rings. The UV spectrum showed absorption maxima at 221 (sh 4.49) and 285 nm (3.88), similar to those of **1**. The ^{1}H-NMR spectrum of **5** indicated the presence of two 3,3-dimethylallyl groups, a 3,3-dimethylallyloxy moiety, a 1,1-dimethylallyl group, three aromatic protons, and 1,3-diphenylpropane moiety: δ 1.66 (6H, s), 1.70, 1.71 (each 3H, s), 3.24 (2H, d, J=6 Hz), 3.36 (2H, d, J=6 Hz), 4.98 (1H, t, J=6 Hz), 5.11 (1H, t, J=6 Hz); δ 1.74, 1.78 (each 3H, s), 4.51 (2H, d, J=7 Hz), 5.47 (1H, t, J=7 Hz); δ 1.36 (6H, s), 5.27 (1H, d, J=11 Hz), 5.32 (1H, d, J=18 Hz), 6.16 (1H, dd, J=11 and 18 Hz); δ 6.30 (1H, s), 6.59 (1H, s), 6.94 (1H, s); δ 1.84 (2H, dd, J=7 and 8 Hz), 2.58 (2H, t, J=8 Hz), 2.60 (2H, t, J=7 Hz). The ^{1}H-NMR spectrum also indicated the presence of three protons of hydroxyl groups as follows: δ 4.61, 5.62, 5.72 (each 1H, br s). The MS of **5** showed

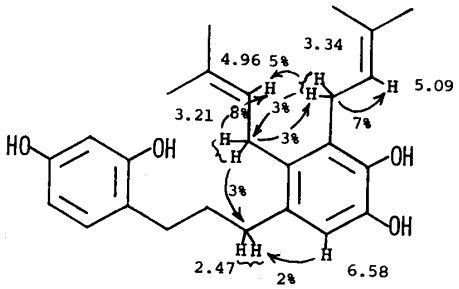

Fig. 4. NOE Results for Kazinol F (Acetone-d_6+D_2O)

%: Increase of signal area.

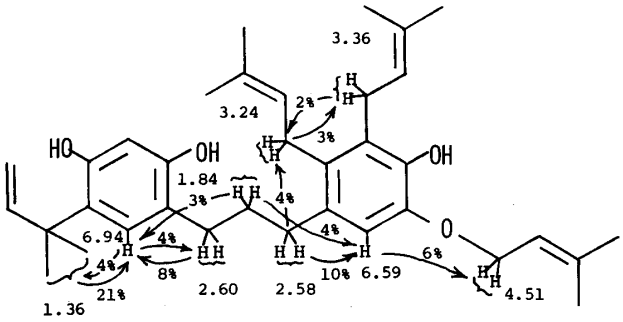

Fig. 5. NOE Results for Kazinol G ($CDCl_3$)

%: Increase of signal area.

significant fragments[9] at *m/z* 259 (**9**) and 191 (**10**). In the ^{13}C-NMR spectrum of **5**, the chemical shift values of the carbon atoms of the 1,3-diphenylpropane skeleton as well as of two 3,3-dimethylallyl groups and a 1,1-dimethylallyl group were similar to those of the relevant carbon atoms of **1** except those of the carbon atoms at C-1″, -2″, -3″, and -4″. These results suggest that the structure of kazinol G is represented by the formula **5**. This assumption was further supported by the NOE: (1) at the C-17″ protons (δ 4.51) when the aromatic proton at C-2″ (δ 6.59) was irradiated, (2) at the C-2″ and C-12″ (δ 3.24) protons when the C-3 protons (δ 2.58) were irradiated, (3) at the C-7″ protons (δ 3.36) when the C-12″ protons were irradiated, (4) between the protons at C-7″ and those at C-12″ when the C-7″ protons (δ 3.36) were irradiated, (5) between the protons at C-2 (δ 1.84), that at C-6′ (δ 6.94) and that at C-2″ when the C-2 protons (δ 1.84) were irradiated, (6) between the C-1 protons (δ 2.60) and the C-6′ proton when the C-1 protons (δ 2.60) were irradiated, (7) between the C-6′ proton, the C-1 protons and the methyl protons at C-7′ (δ 1.36) when the C-6′ proton (δ 6.94) was irradiated, and (8) between the C-7′ methyl protons and the C-6′ proton when the C-7′ methyl protons (δ 1.36) were irradiated (Fig. 5). All these results indicated that the structure of kazinol G is represented by **5**.

Kazinol H (**6**) was obtained as an oily substance, $M^+=460.2617$, $C_{30}H_{36}O_4$, $[\alpha]_D^{18}$ +0.53°, exhibiting a positive ferric chloride test, but a negative sodium molybdate test.[7] The IR spectrum of **6** suggested the presence of hydroxyl groups and aromatic rings. The UV spectrum showed absorption maxima at 229 (4.60), 265 (infl. 3.87), 277 (4.05), 286 (4.05), and 320 nm (3.28). As described in the experimental section, the ^{1}H-NMR spectrum of **6** indicated the presence of a 3,3-dimethylallyl group and a 1,1-dimethylallyl group. The ^{1}H-NMR spectrum also indicated the presence of a 2,2-dimethylpyran ring system, five aliphatic protons, and three aromatic protons: δ 1.43, 1.46 (each 3H, s), 5.63 (1H, d, J=10 Hz), 6.49 (1H, d, J=10 Hz); δ 1.86—2.18 (2H, m), 2.70—2.95 (2H, m), 4.90—5.13 (1H, m); δ 6.36 (1H, s), 6.90 (1H, s), 6.96 (1H, s). The MS of **6** showed significant fragments[2,15] at *m/z* 270 (**14**) and 191 (**10**). In the ^{13}C-NMR spectrum of **6**, the chemical shift values of the carbon atoms of the flavan skeleton as well as of a 3,3-dimethylallyl group and 1,1-dimethylallyl group were similar to those of the relevant carbon atoms of **3** except the carbon atoms at C-4′ and -5′. (±)-Kazinol H was derived from kazinol K (**7**) by treatment with DDQ. From the above results, kazinol H is represented by the formula **6**.

Kazinol K (**7**) was obtained as an oily substance, $M^+=462.2778$, $C_{30}H_{38}O_4$, exhibiting a positive ferric chloride test, but a negative sodium molybdate test.[7] The IR spectrum of **7** suggested the presence of hydroxyl groups and aromatic rings. Treatment of **7** with dimethyl sulfate and potassium carbonate in acetone gave a trimethyl ether (**7a**). The UV spectrum was similar to that of **6**, showing absorption maxima at 226 (4.45), 266 (sh 4.00), 277 (4.18), 285 (4.16), and 324 nm (3.34). As described in the experimental section, the ^{1}H-NMR spectrum of

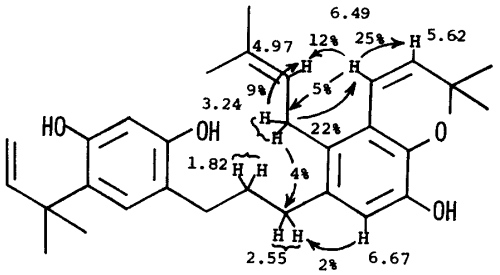

Fig. 6. NOE Results for Kazinol K ($CDCl_3$)
%: Increase of signal area.

7 indicated the presence of a 3,3-dimethylallyl group, a 1,1-dimethylallyl group, a 2,2-dimethylpyran ring system, 1,3-diphenylpropane moiety, and three aromatic protons. The MS of **7** showed a significant fragment at *m/z* 191 (**10**).[9] In the ^{13}C-NMR spectrum of **7** the chemical shift values of the carbon atoms of a 1,3-diphenylpropane skeleton as well as of a 3,3-dimethylallyl group and a 1,1-dimethylallyl group were similar to those of the relevant carbon atoms of **1** except those of the carbon atoms at C-4″ and -5″. In the ^{13}C-NMR spectrum of **7a**, the signals of the methoxyl carbon atoms appeared at δ 55.5 (×2), and 56.4 ppm. This result suggests that all the methoxyl group of **7a** are mono-*ortho*-substituted.[13] The substitution pattern of the B ring of **7** was supported by the NOE: (1) at the C-3 protons (δ 2.55) when the aromatic proton at C-2″ (δ 6.67) was irradiated, (2) at the C-3, C-13″ (δ 4.97), and C-7″ (δ 6.49) protons when the C-12″ protons (δ 3.24) were irradiated, and (3) between the C-7″ proton and the C-12″, C-13″, and C-8″ (δ 5.62) protons when the C-7″ proton (δ 6.49) was irradiated (Fig. 6). The IR and ^{13}C-NMR spectra of the flavan derivative (**6**), which was obtained by treatment of **7** with DDQ, were identical with those of kazinol H. From the above results, kazinol K is represented by the formula **7**.

It is noteworthy that the new compounds described in this paper have a unique substitution pattern in the B ring, that is a 3,4-dihydroxy-5,6-bis(3,3-dimethylallyl)phenyl moiety, and also that kazinol C (**1**) and two other compounds (**3**, **5**) have two 3,3-dimethylallyl groups and a 1,1-dimethylallyl group in the molecule.

Experimental

All melting points are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were measured with tetramethylsilane (TMS) as an internal reference. Chemical shifts are expressed in ppm downfield from TMS and coupling constants (*J*) in Hz. Abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, sh=shoulder, infl.=inflection. The following instruments were used: melting points, Yazawa micromelting point apparatus (hot-stage type); UV spectra, Hitachi 340 UV spectrometer; IR spectra, Hitachi 260-30 IR spectrometer; ^{1}H-NMR spectra, Hitachi R-900 FT NMR spectrometer, JEOL JNM 4H-100 and GX-400 FT NMR spectrometers and Varian XL-200 FT NMR spectrometer; ^{13}C-NMR spectra, JEOL GX-270, GX-400, and Hitachi R-900 FT NMR spectrometers; optical rotation, JASCO DIP-4; CD spectra, JASCO J-20 ORD spectrometer. For TLC and preparative TLC, Wakogel B-5FM and B-5F were used, and for column chromatography, Wakogel C-200.

Isolation of Kazinols C (1), D (2), E (3), F (4), G (5), H (6), and K (7)——The dried root bark (1.0 kg) of *Broussonetia kazinoki* SIEB., collected in the vicinity of Shimokawara, Moroyama Town, Saitama Prefecture in May 1984, was finely cut and extracted with *n*-hexane and then with benzene. Evaporation of the *n*-hexane extract and the benzene extract to dryness yielded 28.0 g and 44.0 g of residue, respectively. The *n*-hexane extract (28.0 g) was chromatographed on silica gel (230 g) with benzene–$(CH_3)_2CO$ as an eluent, each fraction being monitored by TLC. One of the fractions eluted with benzene (1370 mg) was fractionated by preparative TLC (solvent system, $CHCl_3$: Et_2O = 12 : 1, *n*-hexane : Et_2O = 1 : 1) to give kazinol E (**3**, 650 mg). One of the fractions eluted with benzene (1314 mg) was fractionated by preparative TLC (*n*-hexane : Et_2O = 2 : 1, AcOEt : $CHCl_3$ = 2 : 50, AcOEt : *n*-hexane = 1 : 3) to give kazinol G (**5**, 52 mg). One of the fractions eluted with benzene (746 mg) was fractionated by preparative TLC (*n*-hexane : Et_2O = 2 : 1, AcOEt : *n*-hexane = 1 : 3, $CHCl_3$ only) to give kazinol H (**6**, 17 mg). The fractions eluted with benzene containing 1% $(CH_3)_2CO$ were evaporated to give the residue (1.68 g), which was fractionated by preparative TLC ($(CH_3)_2CO$: *n*-hexane = 1 : 3, *n*-hexane : Et_2O = 1 : 1, $CHCl_3$: Et_2O = 4 : 1) to give kazinol K (**7**, 176 mg). One of the fractions eluted with benzene containing 3% $(CH_3)_2CO$ (1728 mg) was fractionated by preparative TLC (benzene : Et_2O = 3 : 1, $CHCl_3$: Et_2O = 5 : 1, benzene : AcOEt = 4 : 1) to give kazinol C (**1**, 420 mg).

The same fraction (1728 mg) was also fractionated by preparative TLC (benzene : Et_2O = 3 : 1, $CHCl_3$ only, $CHCl_3$: AcOEt = 3 : 1) to give kazinol D (**2**, 370 mg). A part of the benzene extract (2.1 g) was fractionated by preparative TLC (benzene : Et_2O = 3 : 1, *n*-hexane : Et_2O = 1 : 3, $CHCl_3$: $(CH_3)_2CO$ = 5 : 2) to give kazinol F (**4**, 2 mg).

Kazinol C (1)——Compound **1** was obtained as an oily substance. $FeCl_3$ test (brown), Na_2MoO_4 test (orange). UV λ_{max}^{EtOH} nm (log ε): 218 (4.59), 286 (3.97). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3650 (sh), 3600 (sh), 3530 (br), 1640 (sh), 1635 (sh), 1625, 1600 (sh). High-resolution MS, Calcd for $C_{30}H_{40}O_4$ (M^+), *m/z* 464.2925. Found: *m/z* 464.2924. MS: *m/z* 464 (M^+), 408 ($M^+ - C_4H_8$), 396 ($M^+ - C_5H_8$), 340 ($396 - C_4H_8$), 273 ($M^+ - 191$), 259 (**8**), 245 (**9**), 205 ($M^+ - 259$), 203 ($259 - C_4H_8$), 191 (**10**), 123 ($191 - C_5H_8$). ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.38 (6H, s, $C_{7'}$-CH_3 × 2), 1.66, 1.70, 1.72, 1.78 (each 3H, s, $C_{9''}$- and $C_{14''}$-CH_3), 1.82 (2H, quintet, J=7, C_2-H × 2), 2.55 (2H, t, J=7, C_3-H × 2), 2.59 (2H, t, J=7, C_1-H × 2), 3.23 (2H, d, J=7, $C_{12''}$-H × 2), 3.34 (2H, d, J=7, $C_{7''}$-H × 2), 4.96 (1H, t, J=7, $C_{13''}$-H), 5.12 (1H, t, J=7, $C_{8''}$-H), 5.25 (1H, d, J=10, $C_{11'}$-H), 5.31 (1H, d, J=18, $C_{11'}$-H), 5.33 (2H, br s, OH × 2, disappeared on addition of D_2O), 5.66, 5.78 (each 1H, br s, OH, disappeared on addition of D_2O), 6.16 (1H, dd, J=10, 18, $C_{10'}$-H), 6.30 (1H, s, $C_{3'}$-H), 6.61 (1H, s, $C_{2''}$-H), 6.93 (1H, s, $C_{6'}$-H). ^{13}C-NMR (22.6 MHz): Table I.

Kazinol C Tetramethyl Ether (1a)——A mixture of **1** (101 mg), $(CH_3)_2SO_4$ (0.5 ml) and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 1 h, and treated as usual. The product was purified by preparative TLC (Et_2O : *n*-hexane = 1 : 5) to give the tetramethyl ether (**1a**, 40 mg). The compound **1a** was obtained as an oily substance. $FeCl_3$ test (negative). MS: *m/z* 520 (M^+). ^{13}C-NMR ($CDCl_3$, 22.6 MHz) δ: 18.0 ($C_{10''}$ and $C_{15''}$), 25.7 ($C_{11''}$ and $C_{16''}$), 25.9 ($C_{12''}$), 27.5 ($C_{8'}$ and $C_{9'}$), 27.7 ($C_{7''}$), 30.2 (C_2), 31.8 (C_1), 33.5 (C_3), 40.0 ($C_{7'}$), 55.4 (OCH_3 × 2), 55.7 (OCH_3), 60.6 (OCH_3), 96.8 ($C_{3'}$), 109.4 ($C_{11'}$), 111.4 ($C_{2''}$), 121.8 ($C_{1'}$), 124.0 ($C_{8''}$), 124.3 ($C_{13''}$), 128.2 ($C_{5'}$), 128.4 ($C_{6'}$), 130.7 ($C_{5''}$), 130.9 ($C_{6''}$ and $C_{14''}$), 134.5 ($C_{9''}$), 136.8 ($C_{1''}$), 145.5($C_{3''}$), 148.6 ($C_{10'}$), 150.6 ($C_{4''}$), 156.6 ($C_{2'}$), 157.3 ($C_{4'}$).

Acetylation of Kazinol C (1)——Kazinol C (**1**, 30 mg) was acetylated with Ac_2O (1.5 ml) and pyridine (0.5 ml) at room temperature for 3 min. The reaction mixture was treated as usual, and the product was purified by preparative TLC (Et_2O : *n*-hexane = 1 : 1) to give a triacetate (**1b**, 19.0 mg) and a tetraacetate (**1c**, 11.8 mg). Kazinol C triacetate (**1b**) was obtained as an oily substance. MS: *m/z* 590 (M^+). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ: 1.41 (6H, s, $C_{7'}$-CH_3 × 2), 1.66 (12H, s, $C_{9''}$-CH_3 × 2 and $C_{14''}$-CH_3 × 2), 1.84 (2H, quintet, J=7, C_2-H × 2), 2.23, 2.26, 2.28 (each 3H, s, OAc), 2.53 (2H, t, J=7, C_1-H × 2), 2.61 (2H, t, J=7, C_3-H × 2), 3.26 (2H, d, J=7, $C_{12''}$-H × 2), 3.29 (2H, d, J=7, $C_{7''}$-H × 2), 4.99 (2H, t, J=7, $C_{8''}$- and $C_{13''}$-H), 5.33 (1H, d, J=10, $C_{11'}$-H), 5.38 (1H, d, J=18, $C_{11'}$-H), 6.20 (1H, dd, J=10, 18, $C_{10'}$-H), 6.56 (1H, s, $C_{3'}$-H), 6.90 (1H, s, $C_{2''}$-H), 7.10 (1H, s, $C_{6'}$-H). Kazinol C tetraacetate (**1c**) was obtained as an oily substance. MS: *m/z* 632 (M^+). ^{1}H-NMR ($CDCl_3$, 200 MHz) δ: 1.41 (6H, s, $C_{7'}$-CH_3 × 2), 1.67 (6H, s, $C_{9''}$- and $C_{14''}$-CH_3), 1.70 (6H, s, $C_{9''}$- and $C_{14''}$-CH_3), 1.87 (2H, quintet, J=7, C_2-H × 2), 2.20, 2.23, 2.27, 2.28 (each 3H, s, OAc), 2.60 (2H, t, J=7, C_3-H × 2), 2.64 (2H, t, J=7, C_1-H × 2), 3.26 (2H, d, J=7, $C_{12''}$-H × 2), 3.30 (2H, d, J=7, $C_{7''}$-H × 2), 4.99 (2H, t, J=7, $C_{8''}$- and $C_{13''}$-H), 5.00 (1H, d, J=10, $C_{11'}$-H), 5.03 (1H, d, J=18, $C_{11'}$-H), 5.99 (1H, dd, J=10, 18, $C_{10'}$-H), 6.79 (1H, s, $C_{3'}$-H), 6.91 (1H, s, $C_{2''}$-H), 7.26 (1H, s, $C_{6'}$-H).

Acidic Treatment of Kazinol C (1) (Formation of Kazinol D (2) and Other Compounds from 1)——A mixture of **1** (52.0 mg) and 35% HCl (3 ml) in MeOH (15 ml) was kept at 60 °C for 2 h, and treated as usual. The product was purified by preparative TLC (*n*-hexane : AcOEt = 2 : 1) to give **1d** (4.5 mg), **1e** (14.4 mg), **1f** (9.6 mg), and **1g** (13.0 mg). Compound **1d** was obtained as an oily substance. MS: *m/z* 464 (M^+), 259, 245, 205, 191. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.25 (3H, s, $C_{7'}$-CH_3), 1.32 (6H, s, $C_{9''}$-CH_3 × 2), 1.38 (3H, d, J=7, $C_{10'}$-CH_3), 1.66 (3H, s, $C_{7'}$-CH_3), 1.70 (6H, s, $C_{14''}$-CH_3 × 2), 1.80 (2H, t, J=7, $C_{8''}$-H × 2), 1.60—1.90 (2H, m, C_2-H × 2), 2.45—2.75 (2H, m, $C_{7''}$-H × 2), 2.58 (2H, t, J=7, C_3-H × 2), 2.64 (2H, t, J=7, C_1-H × 2), 3.17 (2H, d, J=7, $C_{12''}$-H × 2), 4.30 (1H, q, J=7, $C_{10'}$-H), 4.72 (1H, br s, OH), 4.92 (1H, t, J=7, $C_{13''}$-H), 5.44 (1H, br s, OH), 6.21 (1H, s, $C_{3'}$-H), 6.62 (1H, s, $C_{2''}$-H), 6.75 (1H, s, $C_{6'}$-H). Compound **1e** thus obtained was identical with kazinol D (**2**) on the basis of IR and ^{1}H-NMR spectral comparisons. Compound **1f** was obtained as an oily substance. MS: *m/z* 496 (M^+), 464, 396, 259, 245, 217, 205, 191, 123. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.23 (6H, s, $C_{14''}$-CH_3 × 2), 1.34 (6H, s, $C_{9''}$-CH_3 × 2), 1.42 (6H, s, $C_{7'}$-CH_3 × 2), 1.50—1.95 (4H, m, C_2-H × 2 and $C_{13''}$-H × 2), 1.82 (2H, t, J=7, $C_{8''}$-H × 2), 2.30—2.80 (8H, m, C_1-H × 2, C_3-H × 2, $C_{7''}$-H × 2, and $C_{12''}$-H × 2), 3.26 (3H, s, $C_{14''}$-OCH_3), 5.26 (1H, d, J=10, $C_{11'}$-H), 5.29 (1H, d, J=18, $C_{11'}$-H), 6.16 (1H, dd, J=10, 18, $C_{10'}$-H), 6.28 (1H, s, $C_{3'}$-H), 6.64 (1H, s, $C_{2''}$-H), 6.92 (1H, s, $C_{6'}$-H). Compound **1g** was obtained as an oily substance. MS: *m/z* 496 (M^+), 464, 259, 245, 217, 205, 191, 123. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.20 (6H, s, $C_{9''}$-CH_3 × 2), 1.39 (6H, s, $C_{7'}$-CH_3 × 2), 1.67, 1.72 (each 3H, s, $C_{14''}$-CH_3), 1.60—1.90 (4H, m, C_2-H × 2 and $C_{8''}$-H × 2), 2.40—2.80 (6H, m, C_1-H × 2, C_3-H × 2, and $C_{7''}$-H × 2), 3.21 (2H, d, J=7, $C_{12''}$-H × 2), 3.28 (3H, s, $C_{9''}$-OCH_3), 4.96 (1H, t, J=7, $C_{13''}$-H), 5.24 (1H, d, J=10, $C_{11'}$-H), 5.29 (1H, d, J=18, $C_{11'}$-H), 5.50 (1H, br s, OH), 5.77 (2H, br s, OH × 2), 6.15 (1H, dd, J=10, 18, $C_{10'}$-H), 6.29 (1H, s, $C_{3'}$-H), 6.63 (1H, s, $C_{2''}$-H), 6.92 (1H, s, $C_{6'}$-H).

Treatment of Kazinol C (1) with DDQ [Formation of Kazinol E (3) from 1]——A mixture of **1** (9.8 mg) and DDQ (1.5 mg) in dry benzene (1.5 ml) was kept at room temperature for 18 h. The reaction product was purified by preparative TLC (*n*-hexane : Et_2O = 1 : 1) to give an amorphous powder (**3**, 3.9 mg). Compound **3** thus obtained was identical with kazinol E on the basis of MS, IR, ^{1}H-NMR, and ^{13}C-NMR spectral comparisons.

Kazinol D (2)——Compound **2** was obtained as an oily substance. $FeCl_3$ test (brown), Na_2MoO_4 test (negative). UV λ_{max}^{EtOH} nm (log ε): 221 (4.67), 230 (infl. 4.07), 283 (3.91). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3615, 3570, 3500, 1645, 1625, 1600. High-resolution MS, Calcd for $C_{30}H_{40}O_4$ (M^+), *m/z* 464.2925. Found: *m/z* 464.2927. MS: *m/z* 464 (M^+), 396 ($M^+ - C_5H_8$), 340 ($396 - C_4H_8$), 273 ($M^+ - 191$), 259, 245, 205 ($M^+ - 259$), 203 ($259 - C_4H_8$), 191 (**10**), 123 ($191 - C_5H_8$). ^{1}H-

NMR ($CDCl_3$, 100 MHz) δ: 1.32 (6H, s, $C_{9''}$-CH_3 × 2), 1.39 (6H, s, $C_{7'}$-CH_3 × 2), 1.66, 1.71 (each 3H, s, $C_{14''}$-CH_3), 1.60—1.90 (2H, m, C_2-H × 2), 1.80 (2H, t, J=7, $C_{8''}$-H × 2), 2.45—2.75 (6H, m, C_1-H × 2, C_3-H × 2 and $C_{7''}$-H × 2), 3.18 (2H, br d, J=7, $C_{12''}$-H × 2), 4.92 (1H, br t, J=7, $C_{13''}$-H), 5.23 (1H, d, J=10, $C_{11'}$-H), 5.27 (1H, d, J=18, $C_{11'}$-H), 6.14 (1H, dd, J=10, 18, $C_{10'}$-H), 6.28 (1H, s, $C_{3'}$-H), 6.63 (1H, s, $C_{2''}$-H), 6.91 (1H, s, $C_{6'}$-H). ^{13}C-NMR (22.6 Hz): Table I.

Kazinol D Trimethyl Ether (2a)——A mixture of **2** (100 mg), $(CH_3)_2SO_4$ (0.5 ml) and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 2 h, and treated as usual. The product was purified by preparative TLC (*n*-hexane : $CHCl_3$ = 1 : 1) to give kazinol D trimethyl ether (**2a**, 82 mg). Compound **2a** was obtained as an oily substance. $FeCl_3$ test (negative). MS: *m/z* 506 (M^+). ^{13}C-NMR ($CDCl_3$, 22.6 MHz) δ: 17.9 ($C_{15''}$), 20.6 ($C_{7''}$), 25.7 ($C_{16''}$), 26.6 ($C_{10''}$ and $C_{11''}$), 27.5 ($C_{8''}$, $C_{9''}$, and $C_{12''}$), 30.0 (C_2), 31.9 (C_3), 33.2 (C_1 and $C_{8''}$), 39.9 ($C_{7'}$), 55.4 (OCH_3 × 2), 56.0 (OCH_3), 73.0 ($C_{9''}$), 96.7 ($C_{3'}$), 109.4 ($C_{11'}$), 110.9 ($C_{2''}$), 120.4 ($C_{5''}$), 121.8 ($C_{1'}$), 123.5 ($C_{13''}$), 128.1 ($C_{5'}$), 128.4 ($C_{6'}$), 129.8 ($C_{6''}$), 131.0 ($C_{14''}$), 131.3 ($C_{1''}$), 141.8 ($C_{4''}$), 146.8 ($C_{3''}$), 148.5 ($C_{10'}$), 156.5 ($C_{2'}$), 157.2 ($C_{4'}$).

Kazinol E (3)——Compound **3** was crystallized from $CHCl_3$ to give colorless needles, mp 147 °C, $[\alpha]_D^{18}$ +0.30° (c=0.41, $CHCl_3$). $FeCl_3$ test (dark green). Na_2MoO_4 test (orange). UV λ_{max}^{EtOH} nm (log ε): 224 (4.92), 232 (infl. 4.36), 288 (3.91). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (sh), 3550, 3490, 1625, 1585. High-resolution MS, Calcd for $C_{30}H_{38}O_4$ (M^+), *m/z* 462.2768. Found: *m/z* 462.2803. MS: *m/z* 462 (M^+), 406 ($M^+ - C_4H_8$), 394 ($M^+ - C_5H_8$), 272 (**11**), 271, 191 (**10**). ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.38 (6H, s, C_9-CH_3 × 2), 1.65 (9H, s, C_{16}-CH_3 × 2 and C_{21}-CH_3 or C_{16}-CH_3 and C_{21}-CH_3 × 2), 1.76 (3H, s, C_{16}-CH_3 or C_{21}-CH_3), 1.70—2.10 (2H, m, C_3-H × 2), 2.62—2.88 (2H, m, C_4-H × 2), 3.31 (4H, br d, J=7, C_{14}-H × 2 and C_{19}-H × 2), 4.80—5.10 (3H, m, C_2-, C_{15}-, and C_{19}-H), 5.17 (1H, d, J=10, C_{13}-H), 5.21 (1H, d, J=18, C_{13}-H), 5.60 (1H, br s, OH), 5.75 (2H, br s, OH × 2), 6.07 (1H, dd, J=10, 18, C_{12}-H), 6.31 (1H, s, C_8-H), 6.73 (1H, s, $C_{2'}$-H), 6.83 (1H, s, C_5-H). ^{13}C-NMR (22.6 MHz): Table I. CD spectrum: $[\theta]_{295}$ −99, $[\theta]_{279}$ +66 ($c = 5.3 \times 10^{-4}$, MeOH).

Kazinol F (4)——Compound **4** was crystallized from benzene to give colorless needles, mp 108—109 °C. $FeCl_3$ test (dark green). Na_2MoO_4 test (orange). Gibbs test (blue). UV λ_{max}^{EtOH} nm (log ε): 282 (3.91), 286 (sh 3.89). IR ν_{max}^{KBr} cm^{-1}: 3510, 3380, 3320 (sh), 1610. High-resolution MS, Calcd for $C_{25}H_{32}O_4$ (M^+), *m/z* 396.2299. Found: *m/z* 396.2301. MS: *m/z* 396 (M^+), 340 ($M^+ - C_4H_8$), 259 (**8**), 245 (**9**), 123 (**12**). ^{1}H-NMR ($(CD_3)_2CO$, 400 MHz) δ: 1.65 (6H, s, $C_{9''}$- and $C_{14''}$-CH_3), 1.71, 1.73 (each 3H, s, $C_{9''}$- or $C_{14''}$-CH_3), 1.77 (2H, dd, J=7, 8, C_2-H × 2), 2.49 (2H, t, J=8, C_3-H × 2), 2.59 (2H, t, J=7, C_1-H × 2), 3.23 (2H, d, J=6, $C_{12''}$-H × 2), 3.36 (2H, d, J=7, $C_{7''}$-H × 2), 4.97 (1H, t, J=6, $C_{13''}$-H), 5.10 (1H, t, J=7, $C_{8''}$-H), 6.28 (1H, dd, J=2, 8, $C_{5'}$-H), 6.39 (1H, d, J=2, $C_{3'}$-H), 6.57 (1H, s, $C_{2''}$-H), 6.88 (1H, d, J=8, $C_{6'}$-H). ^{13}C-NMR (22.6 MHz): Table I.

Kazinol F Tetramethyl Ether (4a)——A mixture of **4** (30 mg), $(CH_3)_2SO_4$ (0.2 ml), and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 2 h, and treated as usual. The product was purified by preparative TLC (benzene only) to give kazinol F tetramethyl ether (**4a**, 19 mg). Compound **4a** was obtained as an oily substance. $FeCl_3$ test (negative). MS: *m/z* 452 (M^+). ^{13}C-NMR ($CDCl_3$, 22.5 MHz) δ: 17.9 ($C_{10''}$ and $C_{15''}$), 25.5 ($C_{11''}$), 25.6 ($C_{16''}$), 25.8 ($C_{12''}$), 27.6 ($C_{7''}$), 29.7 (C_2), 31.4 (C_3), 33.2 (C_1), 55.0, 55.1, 55.5, 60.3 (each OCH_3), 98.2 ($C_{3'}$), 103.5 ($C_{5'}$), 111.0 ($C_{2''}$), 122.7 ($C_{1'}$), 123.4 ($C_{8''}$), 123.7 ($C_{13''}$), 129.3 ($C_{5''}$), 130.1 ($C_{6'}$), 130.3 ($C_{6''}$), 130.4 ($C_{14''}$), 133.8 ($C_{9''}$), 136.1 ($C_{1''}$), 144.8 ($C_{3''}$), 149.8 ($C_{4''}$), 157.7 ($C_{2'}$), 158.4 ($C_{4'}$).

Treatment of Kazinol F (4) with DDQ——A mixture of **4** (20 mg) and DDQ (3 mg) in dry Et_2O (3 ml) was kept at room temperature for 18 h. The reaction product was purified by preparative TLC (*n*-hexane : $(CH_3)_2CO$ = 2 : 1) to give **13**. Compound **13** thus obtained was identical with kazinol I isolated from *Broussonetia papyrifera* (L.) VENT. On the basis of MS, IR, ^{1}H-NMR spectral comparisons.

Kazinol G (5)——Compound **5** was obtained as an oily substance. $FeCl_3$ test (brown). Na_2MoO_4 test (negative). UV λ_{max}^{EtOH} nm (log ε): 221 (sh 4.49), 285 (3.88). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3540, 3480, 1625, 1610 (sh). High-resolution MS, Calcd for $C_{35}H_{48}O_4$ (M^+), *m/z* 532.3551. Found: *m/z* 532.3536. MS: *m/z* 532 (M^+), 464 ($M^+ - C_5H_8$), 408 (464 − C_4H_8), 259 (**8**), 191 (**10**), 147, 123. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.36 (6H, s, $C_{7'}$-CH_3 × 2), 1.66 (6H, s, $C_{9''}$- and $C_{14''}$-CH_3), 1.70 (3H, s, $C_{9''}$- or $C_{14''}$-CH_3), 1.71 (3H, s, $C_{9''}$- or $C_{14''}$-CH_3), 1.74, 1.78 (each 3H, s, $C_{19'}$-CH_3), 1.84 (2H, dd, J=7, 8, C_2-H × 2), 2.58 (2H, t, J=8, C_3-H × 2), 2.60 (2H, t, J=7, C_1-H × 2), 3.24 (2H, d, J=6, $C_{12''}$-H × 2), 3.36 (2H, d, J=6, $C_{7''}$-H × 2), 4.51 (2H, d, J=7, $C_{17''}$-H × 2), 4.61 (1H, br s, OH), 4.98 (1H, t, J=6, $C_{13''}$-H), 5.11 (1H, t, J=6, $C_{8''}$-H), 5.27 (1H, d, J=11, $C_{11'}$-H), 5.32 (1H, d, J=18, $C_{11'}$-H), 5.47 (1H, t, J=7, $C_{18''}$-H), 5.62 (1H, br s, OH), 5.72 (1H, br s, OH), 6.16 (1H, dd, J=11, 18, $C_{10'}$-H), 6.30 (1H, s, $C_{3'}$-H), 6.59 (1H, s, $C_{2''}$-H), 6.94 (1H, s, $C_{6'}$-H). ^{13}C-NMR (100.4 MHz): Table I.

Kazinol H (6)——Compound **6** was obtained as an oily substance, $[\alpha]_D^{18}$ +0.53° (c=0.94, MeOH). $FeCl_3$ test (brown). Na_2MoO_4 test (negative). UV λ_{max}^{EtOH} nm (log ε): 229 (4.60), 265 (infl. 3.87), 277 (4.05), 286 (4.05), 320 (3.28). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3490, 1660, 1595, 1585. High-resolution MS, Calcd for $C_{30}H_{36}O_4$ (M^+), *m/z* 460.2612. Found: *m/z* 460.2617. MS: *m/z* 460 (M^+), 445 ($M^+ - CH_3$), 270 (**14**), 255 (270 − CH_3), 191 (**10**), 123 (191 − C_5H_8). ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 1.43 (9H, s, C_9-CH_3 × 2 and C_{16}-CH_3), 1.46 (3H, s, C_{16}-CH_3), 1.67, 1.69 (each 3H, s, C_{21}-CH_3), 1.86—2.18 (2H, m, C_3-H × 2), 2.70—2.95 (2H, m, C_4-H × 2), 3.31 (2H, br d, J=7, C_{19}-H × 2), 4.99 (1H, t, J=7, C_{20}-H), 4.99—5.13 (1H, m, C_2-H), 5.25 (1H, d, J=10, C_{13}-H), 5.29 (1H, d, J=18, C_{13}-H), 5.36 (1H, br s, OH), 5.63 (1H, d, J=10, C_{16}-H), 5.64 (1H, br s, OH), 6.17 (1H, dd, J=10, 18, C_{12}-H), 6.36 (1H, s, C_8-H), 6.49 (1H, d, J=10, C_{14}-H), 6.90 (1H, s, $C_{2'}$-H), 6.96 (1H, s, C_5-H). ^{13}C-NMR (67.8 MHz): Table I.

Kazinol K (7)——Compound **7** was obtained as an oily substance. $FeCl_3$ test (brown). Na_2MoO_4 test (negative). UV λ_{max}^{EtOH} nm (log ε): 226 (4.45), 266 (sh, 4.00), 277 (4.18), 285 (4.16), 324 (3.34). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3550, 3480, 1625, 1600. High-resolution MS, Calcd for $C_{30}H_{38}O_4$ (M^+), *m/z* 462.2768. Found: *m/z* 462.2778. MS: *m/z* 462 (M^+), 447 ($M^+ - CH_3$), 191 (**10**). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.40, 1.42 (each 6H, s, $C_{7''}$-$CH_3 \times 2$ and $C_{9''}$-$CH_3 \times 2$), 1.66, 1.71 (each 3H, s, $C_{14''}$-CH_3), 1.82 (2H, quintet, $J=8$, C_2-H × 2), 2.55 (2H, t, $J=8$, C_3-H × 2), 2.60 (2H, t, $J=8$, C_1-H × 2), 3.24 (2H, d, $J=6$, $C_{12''}$-H × 2), 4.97 (1H, t, $J=6$, $C_{13''}$-H), 5.16 (1H, br s, OH, disappeared on addition of D_2O), 5.26 (1H, dd, $J=1$, 11, $C_{11'}$-H), 5.31 (1H, dd, $J=1$, 18, $C_{11'}$-H), 5.40 (1H, br s, OH, disappeared on addition of D_2O), 5.62 (1H, d, $J=10$, $C_{8''}$-H), 5.78 (1H, br s, OH, disappeared on addition of D_2O), 6.16 (1H, dd, $J=11$, 18, $C_{10'}$-H), 6.30 (1H, s $C_{3'}$-H), 6.49 (1H, d, $J=10$, $C_{7''}$-H), 6.67 (1H, s, $C_{2''}$-H), 6.94 (1H, s, $C_{6'}$-H). ^{13}C-NMR (100.4 MHz): Table I.

Kazinol K Trimethyl Ether (7a)——A mixture of **7** (20 mg), $(CH_3)_2SO_4$ (0.2 ml), and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 2 h, and treated as usual. The product was purified by preparative TLC (benzene only) to give kazinol K trimethyl ether (**7a**, 12 mg). Compound **7a** was obtained as an oily substance. $FeCl_3$ test (negative). MS: *m/z* 504 (M^+). ^{13}C-NMR ($CDCl_3$, 67.8 MHz) δ: 17.9 ($C_{15''}$), 25.6 ($C_{16''}$), 26.8 ($C_{12''}$), 27.4 ($C_{8'}$, $C_{9'}$, $C_{10''}$, and $C_{11''}$), 29.9 (C_2), 31.8 (C_3), 33.1 (C_1), 39.9 ($C_{7'}$), 55.5 ($OCH_3 \times 2$), 56.4 (OCH_3), 74.9 ($C_{9''}$), 96.8 ($C_{3'}$), 109.3 ($C_{11'}$), 113.8 ($C_{2''}$), 120.2 ($C_{5''}$), 120.6 ($C_{7''}$), 121.6 ($C_{1'}$), 123.9 ($C_{13''}$), 127.6 ($C_{6''}$), 128.0 ($C_{5'}$), 128.2 ($C_{6'}$), 130.7 ($C_{8''}$ and $C_{14''}$), 132.5 ($C_{1''}$), 140.3 ($C_{4''}$), 146.3 ($C_{3''}$), 148.5 ($C_{10'}$), 156.4 ($C_{2'}$), 157.1 ($C_{4'}$).

Treatment of Kazinol K with DDQ [Formation of Kazinol H (6) from 7]——A mixture of **7** (97 mg) and DDQ (15 mg) in dry benzene (15 ml) was kept at room temperature for 36 h. The reaction product was purified by preparative TLC ($(CH_3)_2CO$: *n*-hexane = 1 : 3) to give **6** (6.6 mg). Compound **6** thus obtained was identical with authentic **6** on the basis of MS, IR, and ^{13}C-NMR comparisons.

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References and Notes

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