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Components of *Broussonetia kazinoki* SIEB. (2). Structures of Four New Isoprenylated 1,3-Diphenylpropane Derivatives, Kazinols J, L, M, and N[1]

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A new isoprenylated 1,3-diphenylpropane derivative, kazinol L, was isolated from the extract of the root bark of *Broussonetia kazinoki* SIEB. (Japanese name, "Himekōzo," Moraceae), and three new isoprenylated 1,3-diphenylpropane derivatives, kazinols J, M, and N were isolated from the cortex. The structures of kazinols J, L, M, and N were shown to be **1**, **2**, **3**, and **4**, respectively, on the basis of spectral data.

Keywords——*Broussonetia kazinoki*; Moraceae; 1,3-diphenylpropane; kazinol J; kazinol L; kazinol M; kazinol N

Previously we reported the structure determination of two new isoprenylated flavans and five new isoprenylated 1,3-diphenylpropane derivatives obtained from the root bark of *Broussonetia kazinoki* SIEB. (Japanese name "Himekōzo", Moraceae).[2] In the course of extended studies of the components of the plant, kazinol L was isolated from the root bark, and kazinols J, M, and N were isolated from the cortex. In this paper we report the structure determination of these compounds. The *n*-hexane extract of the root bark was dissolved in methanol. The methanol extract was fractionated sequentially by column chromatography and preparative thin-layer chromatography (TLC) on silica gel to give kazinol L (**2**). The benzene extract of the cortex was dissolved in methanol. The methanol extract was fractionated sequentially by column chromatography and preparative TLC to give kazinols J (**1**), M (**3**), and N (**4**).

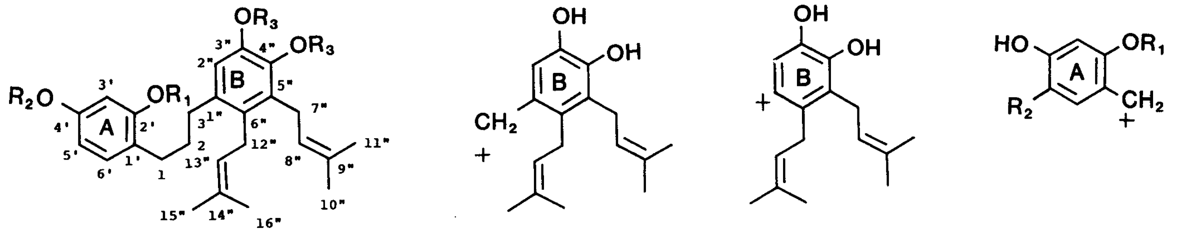
Kazinol J (**1**) was obtained as colorless needles, $M^+ = 410.2470$, $C_{26}H_{34}O_4$, exhibiting a positive ferric chloride test and sodium molybdate test.[3] The infrared (IR) spectrum of **1** suggested the presence of hydroxyl groups [3550, 3210 (br) cm^{-1}] and aromatic rings [1610, 1510 cm^{-1}]. The ultraviolet (UV) spectrum of **1** showed absorption maxima at 282 (log $\varepsilon = 4.04$) and 288 (sh, 4.00) nm, which indicated the presence of an unconjugated aromatic system.[2,4] The proton nuclear magnetic resonance (^1H-NMR) spectrum of **1** indicated the presence of two 3,3-dimethylallyl groups [δ 1.66, 1.70, 1.72, 1.80 (each 3H, br s), 3.22 (2H, br d, $J = 6$ Hz), 3.34 (2H, br d, $J = 6.5$ Hz), 4.95 (1H, br t, $J = 6$ Hz), 5.13 (1H, br t, $J = 6.5$ Hz)], a methoxyl group [δ 3.75 (3H, s)], and a 1,3-disubstituted propane moiety [δ 1.76 (2H, m), 2.51 (2H, t, $J = 8$ Hz), 2.57 (2H, t, $J = 7.5$ Hz)]. The ^1H-NMR spectrum also indicated the presence of ABC type aromatic protons [δ 6.32 (1H, dd, $J = 2.5$ and 8 Hz), 6.37 (1H, d, $J = 2.5$ Hz), 6.93 (1H, d, $J = 8$ Hz)], and an aromatic proton [δ 6.61 (1H, s)]. The mass spectrum (MS) of **1** showed significant fragments at m/z 259 (**5**), 245 (**6**), and 137 (**7**).[2,4] From the above spectral data and the result of the sodium molybdate test, it was suggested that kazinol J is a 1,3-diphenylpropane derivative having a hydroxyl group and a methoxyl group in one of the phenyl moieties and having two 3,3-dimethylallyl groups and *ortho*-dihydroxyl

Table I. ^{13}C-NMR Data of Kazinols J (**1**), L (**2**), M (**3**), N (**4**), and Related Compounds in $CDCl_3$

Carbon No.	**1**	**2**	**2a**	**3**	**3a**	**4**	**8**[a]	**12**[a]	**13**[a]		**11**[b]
C-1	33.5[c]	32.3[c]	33.2[c]	32.3[c]	33.0[c]	32.6[c]	33.6[c]	32.7[c]	32.6[c]	(2)[i]	74.8
C-2	30.2	29.5	30.1	28.9	29.6	29.5	30.4	29.7	29.5	(3)	24.8
C-3	32.9[c]	31.9[c]	32.5[c]	31.1[c]	31.6[c]	31.4[c]	33.1[c]	31.7[c]	31.4[c]	(4)	29.9
C-1′	121.6	119.4	121.5	120.0	122.7	122.2	120.5	120.5	119.5	(4a)	113.9
C-2′	158.5	152.9[d]	156.7[d]	153.9[d]	157.6[d]	157.6	157.3[d]	153.7[d]	152.8[d]	(8a)	156.1[c]
C-3′	99.3	104.4	97.0	102.5	98.1	98.5	103.4	104.8	104.3	(8)	103.7
C-4′	156.9	152.4[d]	157.3[d]	153.7[d]	158.4[d]	154.2	156.6[d]	153.3[d]	152.6[d]	(7)	155.1[c]
C-5′	106.9	123.5	128.5	107.1	103.4	106.1	107.3	124.0	123.7	(6)	108.1
C-6′	130.1	127.0	128.5	130.0	129.3	129.8	131.1	127.6	127.0	(5)	130.0
C-7′		39.0	40.1					39.8	39.6		
C-8′		27.1	27.7					27.3	27.1		
C-9′		27.1	27.7					27.3	27.1		
C-10′		147.7	148.6					148.6	147.8		
C-11′		112.6	109.5					112.7	112.5		
C-1″	132.0	134.6	135.2	132.3	131.9	132.7	132.7	132.0	132.3	(1′)	131.6
C-2″	114.1	111.7	108.8	115.1	113.4	115.1	114.6	113.1	115.0	(2′)	125.8
C-3″	142.4	141.1	144.5	141.6	145.7	141.6	143.0	143.0	141.9	(3′)	142.2
C-4″	141.5	138.2	143.5	136.9	139.9	136.8	142.2	139.2	137.0	(4′)	138.6
C-5″	129.9	121.9	124.2	119.2	120.1	119.2	130.4	119.8	119.2	(5′)	119.0
C-6″	127.2	128.4	129.3	126.4	127.1	126.3	127.7	128.9	126.2	(6′)	122.3
C-7″	28.0[e]	105.7	106.1	119.6	119.7	119.7	28.1[e]	20.3	119.6	(14)	115.1
C-8″	124.3[f]	143.8	144.5	129.9	130.1	129.9	124.9[f]	33.2	129.8	(15)	130.1
C-9″	130.1	28.4	28.6	75.5	74.5	75.4	130.7	74.0	75.5	(16)	77.4
C-10″	25.6[g]	123.1	123.9	27.5	27.4	27.4	25.8	26.6	27.5	(17)	28.0
C-11″	17.9[h]	130.4	131.0	27.5	27.4	27.4	18.0	26.6	27.5	(18)	28.2
C-12″	26.1[e]	25.5	25.8	26.6	26.8	26.6	26.2[e]	27.3	26.7	(9)	25.3
C-13″	125.2[f]	17.9	18.1	123.4	123.5	123.5	125.8[f]	123.6	123.6	(10)	122.9
C-14″	130.1			130.3	130.2	130.1	130.7	131.0	130.2	(11)	132.3
C-15″	25.7[g]			25.4	25.5	25.5	25.8	25.7	25.5	(12)	25.7
C-16″	18.0[h]			17.9	17.9	17.9	18.0	17.9	17.9	(13)	17.9
OCH_3	55.3		55.7 (×2) 56.4		55.0 55.1 56.3	54.9					

a) Data from ref. 2. *b*) Data from ref. 11. *c*—*h*) Assignments may be changed in each column. *i*) The numbers are those of the corresponding carbons of **11**.

groups in the other phenyl moiety. In the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **1**, the carbon atoms were assigned by the off-resonance decoupling technique as well as by comparison of the ^{13}C-NMR spectrum of **1** with that of a model compound, kazinol F (**8**)[2] (Table I). The chemical shift values of the carbon atoms of the 1,3-diphenylpropane skeleton, except for C-3′,[5] and those of the carbon atoms of the two 3,3-dimethylallyl groups were similar to those of the relevant carbon atoms of **8**. Treatment of **1** with dimethyl sulfate and potassium carbonate in acetone gave a trimethyl ether (**1a**) which was identical with kazinol F tetramethyl ether.[2] From the above results, two possible structures (**1** and **1′**) were suggested. Discrimination between the structures was achieved by nuclear Overhauser effect (NOE) measurement as follows: when the methyl group at δ 3.75 was irradiated, NOE was observed at the C-3′ proton (δ 6.37). When the proton of the hydroxyl group at δ 5.22 was irradiated, the protons of all the hydroxyl groups were saturated[6] and the irradiation increased the signal areas of the C-3′, C-5′ and C-2″[7] protons (Fig. 2). The NOE was also observed in kazinol J trimethoxymethyl ether (**1b**) at the C-3′,[8] C-

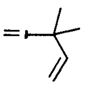


1: $R_1=Me$, $R_2=R_3=H$
1′: $R_1=R_3=H$, $R_2=Me$
1a: $R_1=R_2=R_3=Me$
1b: $R_1=Me$, $R_2=R_3=CH_2OMe$
8: $R_1=R_2=R_3=H$

5

6

7: $R_1=Me$, $R_2=H$
10: $R_1=H$, $R_2=$



15: $R_1=R_2=H$

Fig. 1

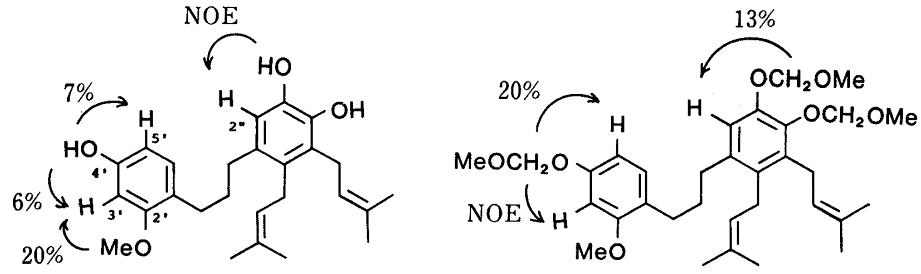
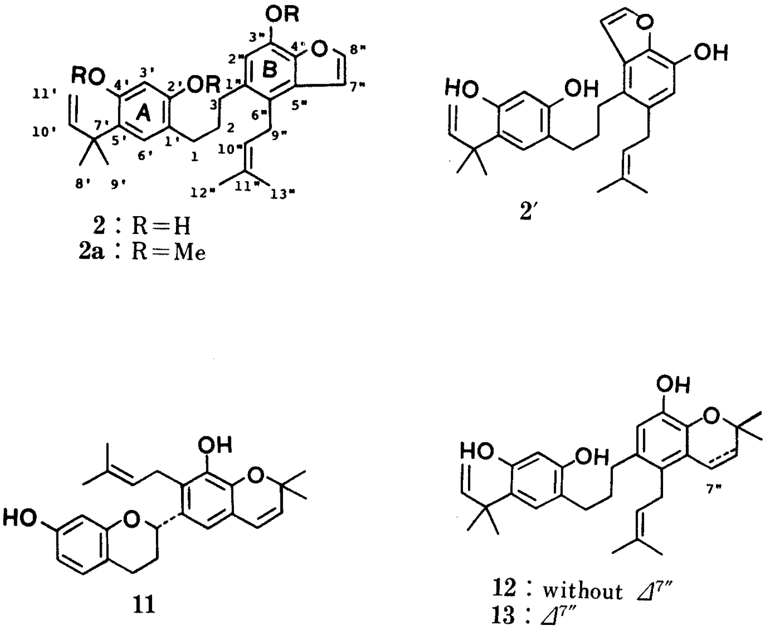


Fig. 2. NOE Values for Kazinol J (**1**) and Kazinol J Trimethoxymethyl Ether (**1b**)

5′, and C-2″ protons when the methylene protons of the methoxymethylene groups at δ 5.14 and 5.15 were irradiated (Fig. 2). All these results indicated that kazinol J is represented by formula **1**.

Kazinol L (**2**) was obtained as an oily substance, $M^+=420.2270$, $C_{27}H_{32}O_4$, exhibiting a positive ferric chloride test, but a negative sodium molybdate test[3] and Gibbs test. The IR spectrum of **2** suggested the presence of hydroxyl groups and aromatic rings. The UV spectrum of **2** showed absorption maxima at 248, 259, and 285 nm. Treatment of **2** with dimethyl sulfate and potassium carbonate in acetone gave a trimethyl ether (**2a**) as an oily substance. The MS of **2a** showed the molecular ion peak at *m*/*z* 462 and exhibited a negative ferric chloride test. The ^{1}H-NMR spectrum of **2** indicated the presence of a 3,3-dimethylallyl group, a 1,1-dimethylallyl group, a 1,3-disubstituted propane moiety, three aromatic protons [δ 6.30, 6.68, and 6.94 (each 1H, s)], and a pair of *cis* olefinic protons [δ 6.73 (1H, d, $J=2$ Hz) and 7.55 (1H, d, $J=2$ Hz)]. The chemical shift values of the *cis* olefinic protons were similar to those of the corresponding protons at the C-2 and C-3 positions of benzofuran [δ 7.51 (C_2-H) and 6.62 (C_3-H)].[9] The MS of **2** showed significant fragments at *m*/*z* 201 (**9**) and 191 (**10**).[2,10] From the above results, it was suggested that kazinol L is a 1,3-disubstituted propane derivative having an isoprenyl and two hydroxyl groups in the phenyl moiety, and an isoprenyl and a hydroxyl group in the benzofuran moiety. In the ^{13}C-NMR spectrum of **2**, the carbon atoms were assigned by the off-resonance decoupling technique, as well as by comparison of the ^{13}C-NMR spectrum of **2** with those of model compounds, such as kazinols B (**11**),[11] D (**12**),[2] and K (**13**).[2] The chemical shift values of the carbon atoms of the 1,3-diphenylpropane skeleton except for the B-ring, and of the carbon atoms of the 1,1-dimethylallyl moiety were similar to those of the relevant carbon atoms of the model compounds **12** and **13**. The chemical shift values of the oxygenated carbon atoms of the B-ring of **2** were similar to those of the carbon atoms at the C-3″ and -4″ positions of **11**, **12**, and **13**. The results suggested that **2** has *ortho*-dioxygenated carbon atoms in the B-ring, and one of the oxygen atoms is part of a



2 : R=H
2a : R=Me

2'

11

12 : without $\Delta^{7''}$
13 : $\Delta^{7''}$

Fig. 3

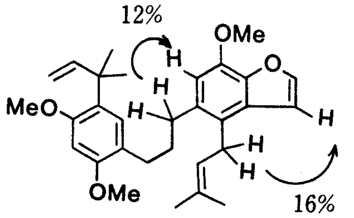
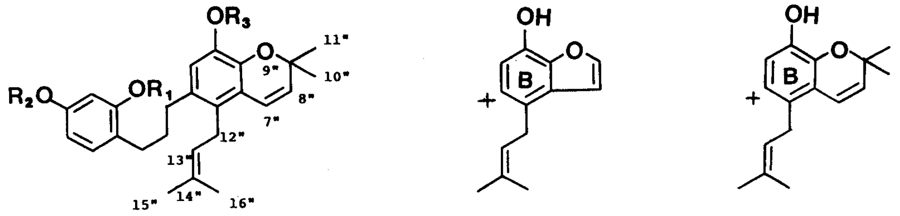


Fig. 4. NOE Values for Kazinol L Trimethyl Ether (**2a**)

hydroxyl group while the other forms an ether linkage. The chemical shift values of the carbon atoms at the C-7'' and -8'' positions were similar to those of the relevant carbon atoms of benzofuran [δ in CS_2: 145.1 (C_2), 106.9 (C_3)][9] (Table I). In the ^{13}C-NMR spectrum of **2a**, the signals of the methoxyl carbon atoms appeared at δ 55.7 ($OCH_3 \times 2$) and 56.4, suggesting that all the methoxyl groups are mono-*ortho*-substituted methoxyl groups.[12] From the above results, the structure of kazinol L seems to be **2** or **2'**. Discrimination between the structures (**2** and **2'**) was achieved by NOE measurements. The NOE was observed in **2a** as follows: 1) at the C-2'' proton (δ 6.63) when the methylene protons at δ 2.70 (C_3-H × 2) were irradiated and 2) at the C-7'' proton (δ 6.71) when the methylene protons at δ 3.45 ($C_{9''}$-H × 2) were irradiated (Fig. 4). All these results indicated that kazinol L is represented by formula **2**.

Kazinol M (**3**) was obtained as an oily substance, $M^+ = 394.2135$, $C_{25}H_{30}O_4$, exhibiting a positive ferric chloride test and Gibbs test but a negative sodium molybdate test.[3] The IR spectrum of **3** suggested the presence of hydroxyl groups and aromatic rings. The UV spectrum of **3** showed absorption maxima at 228, 266 (infl.), 277, 286 (sh), and 325 nm. Treatment of **3** with dimethyl sulfate and potassium carbonate in acetone gave a trimethyl ether (**3a**) as an oily substance. The MS of **3a** showed the molecular ion peak at *m/z* 436, and exhibited a negative ferric chloride test. The ^1H-NMR spectrum of **3** indicated the presence of a 3,3-dimethylallyl group, a 2,2-dimethylpyran ring system [δ 1.41 (6H, s), 5.62 (1H, d, $J = 10$ Hz), and 6.48 (1H, d, $J = 10$ Hz)], and a 1,3-disubstituted propane moiety. The ^1H-NMR spectrum also indicated the presence of ABC type aromatic protons and a singlet aromatic proton [δ 6.65 (1H)]. The chemical shift value of the singlet proton signal was similar to that of the C-2'' proton of **2**. The MS of **3** showed significant fragments at *m/z* 243 (**14**) and 123 (**15**).[2,10] In the ^{13}C-NMR spectrum of **3a**, the signals of the methoxyl carbon atoms



3: $R_1 = R_2 = R_3 = H$

3a: $R_1 = R_2 = R_3 = Me$

4: $R_1 = Me$, $R_2 = R_3 = H$

4′: $R_1 = R_3 = H$, $R_2 = Me$

9

14

Fig. 5

appeared at δ 55.0, 55.1, and 56.3, suggesting the absence of di-*ortho*-substituted methoxyl groups.[12] In the ^{13}C-NMR spectrum of **3**, the chemical shift values of all the carbon atoms, except C-5′ and -6′, were similar to those of the relevant carbon signals of **13** (Table I). The substitution pattern of the B-ring was further supported by NOE measurement as follows: when the methylene protons at δ 3.23 ($C_{12''}$-H × 2) were irradiated, NOE was observed at the C-7″ proton (δ 6.48, 26%). From the above results, the structure of kazinol M is represented by formula **3**.

Kazinol N (**4**) was obtained as an oily substance, $M^+ = 408.2294$, $C_{26}H_{32}O_4$, exhibiting a positive ferric chloride test, and a negative sodium molybdate test.[3] The IR spectrum of **4** suggested the presence of hydroxyl groups and aromatic rings. The UV spectrum of **4** showed absorption maxima at 231, 266 (infl.), 276, 286 (sh), and 325 nm. The ^{1}H-NMR spectrum of **4** indicated the presence of a 3,3-dimethylallyl group, a 2,2-dimethylpyran ring system, and a 1,3-disubstituted propane moiety. The ^{1}H-NMR spectrum also indicated the presence of a methoxyl group, ABC type aromatic protons, and a singlet aromatic proton [δ 6.66 (1H)]. The MS of **4** showed significant fragments at *m/z* 243 (**14**) and 137 (**7**).[2,4] In the ^{13}C-NMR spectrum of **4**, the chemical shift values of carbon atoms of the 1,3-diphenylpropane skeleton except C-1′, -2′, and -3′, as well as the carbon atoms of the 3,3-dimethylallyl group and the 2,2-dimethylpyran ring system, were similar to those of the relevant carbon atoms of **3**. Treatment of **4** with dimethyl sulfate and potassium carbonate in acetone gave a dimethyl ether, which was identical with kazinol M trimethyl ether (**3a**). From the above results, the structure of kazinol N seems to be **4** or **4′**. Discrimination between the structures (**4** and **4′**) was achieved NOE measurement. When the methoxyl proton at δ 3.75 was irradiated, NOE was observed at the C-3′ proton (δ 6.38, 7%), but not at any other proton. When the hydroxyl group at δ 5.26 was irradiated, the proton signals of both the hydroxyl groups at δ 5.26 and 5.38 were saturated[9] and the irradiation increased the areas of the C-3′ proton (7%), the C-5′ proton (10%), and the C-2″ proton (3%) signals. Kazinol N was derived from **1** by treatment with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). From the above results, the structure of kazinol N is represented by formula **4**.

Experimental

Abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, sh = shoulder, and infl. = inflection. The general experimental procedures and instruments used are described in the previous paper.[2]

Isolation of Kazinol L (2)——The dried root bark (5.0 kg) of *Broussonetia kazinoki* SIEB., collected in the Botanical Garden (Yachiyo city, Chiba), Faculty of Pharmaceutical Sciences, Toho University, Japan, in June, 1984, was finely cut and extracted with *n*-hexane. Evaporation of the hexane extract to dryness yielded 80 g of residue, which was dissolved in MeOH, and the MeOH extract (30 g) was chromatographed on silica gel (260 g) using benzene–$CHCl_3$ as an eluent, each fraction being monitored by TLC. Fractions eluted with $CHCl_3$ were evaporated to give the residue (4.0 g), which was fractionated by preparative TLC (solvent systems, benzene : $Et_2O = 2:1$, $CHCl_3 : (CH_3)_2CO = 5:1$, hexane: $(CH_3)_2CO = 2:1$, $CH_2Cl_2 : (CH_3)_2CO = 10:1$) to give kazinol L (**2**, 12 mg).

Isolation of Kazinols J (1), M (3), and N (4)——The dried cortex (6.2 kg) of *Broussonetia kazinoki* SIEB., described above, was finely cut and extracted with *n*-hexane and then with benzene. Evaporation of the hexane and the benzene extract to dryness yielded 123 and 72 g of residues, respectively. The benzene extract (72 g) was dissolved in MeOH, and the MeOH extract (50 g) was chromatographed on silica gel (410 g) using benzene–$(CH_3)_2CO$ as an eluent, each fraction being monitored by TLC. One of the fractions eluted with benzene containing 2% $(CH_3)_2CO$ was evaporated to give the residue (1.5 g), which was fractionated by preparative TLC ($CHCl_3$: $(CH_3)_2CO$ = 5 : 1) to give kazinol J (**1**, 500 mg). One of the fractions eluted with benzene containing 3% $(CH_3)_2CO$ was evaporated to give the residue (0.76 g), which was fractionated by preparative TLC (benzene : AcOEt = 3 : 1, $CHCl_3$: $(CH_3)_2CO$ = 5 : 1, *n*-hexane : $(CH_3)_2CO$ = 5 : 2, CH_2Cl_2 : Et_2O = 5 : 1, $CHCl_3$: MeOH = 10 : 1) to give kazinol M (**3**, 100 mg). One of the fractions eluted with benzene was evaporated to give the residue (1.0 g), which was fractionated by preparative TLC ($CHCl_3$: Et_2O = 6 : 1, *n*-hexane : Et_2O = 5 : 4, CH_2Cl_2 only, *n*-hexane : $(CH_3)_2CO$ = 2 : 1) to give kazinol N (**4**, 100 mg).

Kazinol J (1)——Compound **1** was crystallized from $CHCl_3$ to give colorless needles, mp 116—118 °C. $FeCl_3$ test (brown), Na_2MoO_4 test (orange). UV λ_{max}^{EtOH} nm (log ε): 282 (4.04), 288 (sh 4.00). IR ν_{max}^{KBr} cm^{-1}: 3550, 3210 (br), 1610, 1510. High-resolution MS: Calcd for $C_{26}H_{34}O_4$ (M^+, *m/z*): 410.2455. Found: 410.2470. Calcd for $C_{16}H_{21}O_2$: 245.1540. Found: 245.1545. MS (75 eV) *m/z* (relative intensity): 411 ($M^+ + 1$, 28%), 410 (M^+, 70), 354 (34), 259 (26), 245 (28), 217 (39), 205 (28), 204 (56), 203 (43), 189 (70), 161 (49), 137 (base peak). ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.66, 1.70, 1.72, 1.80 (each 3H, br s, $C_{9''}$- or $C_{14''}$-CH_3), 1.76 (2H, m, C_2-H × 2), 2.51 (2H, t, *J* = 8 Hz, C_3-H × 2), 2.57 (2H, t, *J* = 7.5 Hz, C_1-H × 2), 3.22 (2H, br d, *J* = 6 Hz, $C_{12''}$-H × 2), 3.34 (2H, br d, *J* = 6.5 Hz, $C_{7''}$-H × 2), 3.75 (3H, s, OCH_3), 4.95 (1H, br t, *J* = 6 Hz, $C_{13''}$-H), 4.95 (1H, br s, OH, disappeared on addition of D_2O, overlapping with the signal of $C_{13''}$-H), 5.13 (1H, br t, *J* = 6.5 Hz, $C_{8''}$-H), 5.15—5.35 (2H, br, OH × 2, disappeared on addition of D_2O), 6.32 (1H, dd, *J* = 2.5, 8 Hz, $C_{5'}$-H), 6.37 (1H, d, *J* = 2.5 Hz, $C_{3'}$-H), 6.61 (1H, s, $C_{2''}$-H), 6.93 (1H, d, *J* = 8 Hz, $C_{6'}$-H). The ^{13}C-NMR (100.4 MHz) is described in Table I.

Kazinol J Trimethyl Ether (1a)——A mixture of **1** (14 mg), $(CH_3)_2SO_4$ (0.2 ml), and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 3 h, and treated as usual. The product was purified by preparative TLC ($(CH_3)_2CO$: *n*-hexane = 1 : 2) to give kazinol J trimethyl ether (**1a**, 4.8 mg) as an oily substance. $FeCl_3$ test (negative). MS *m/z*: 452 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2930, 1610, 1585. This product (**1a**) was identical with kazinol F tetramethyl ether on the basis of IR and MS comparisons.

Kazinol J Trimethoxymethyl Ether (1b)——A mixture of **1** (100 mg), CH_3OCH_2Cl (3 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 : $(CH_3)_2CO$ = 5 : 1, Et_2O : *n*-hexane = 1 : 1) to give kazinol J trimethoxymethyl ether (**1b**, 35 mg) as an oily substance. $FeCl_3$ test (negative). MS *m/z*: 542 (M^+). ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.66 (6H, br s, $C_{9''}$-or/and $C_{14''}$-CH_3 × 2), 1.68, 1.72 (each 3H, br s, $C_{9''}$- or $C_{14''}$-CH_3), 1.80 (2H, m, C_2-H × 2), 2.55 (2H, t, *J* = 8 Hz, C_3-H × 2), 2.61 (2H, t, *J* = 7.5 Hz, C_1-H × 2), 3.21 (2H, br d, *J* = 6 Hz, $C_{12''}$-H × 2), 3.40 (2H, br d, *J* = 6 Hz, $C_{7''}$-H × 2), 3.48, 3.49, 3.57, 3.79 (each 3H, s, $-OCH_3$), 4.95 (1H, br t, *J* = 6 Hz, $C_{13''}$-H), 5.07 (1H, br t, *J* = 6 Hz, $C_{8''}$-H), 5.05, 5.14, 5.15 (each 2H, s, $-O-CH_2-O-$), 6.55 (1H, d, *J* = 2 Hz, $C_{3'}$-H), 6.57 (1H, dd, *J* = 2, 9 Hz, $C_{5'}$-H), 6.83 (1H, s, $C_{2''}$-H), 7.01 (1H, d, *J* = 9 Hz, $C_{6'}$-H).

Kazinol L (2)——Compound **2** was obtained as an oily substance. $FeCl_3$ test (brown, coloration was weak and slowly), Na_2MoO_4 test (negative), Gibbs test (negative). High-resolution MS: Calcd for $C_{27}H_{32}O_4$ (M^+, *m/z*): 420.2298. Found: 420.2270. Calcd for $C_{13}H_{13}O_2$ (**9**): 201.0915. Found: 201.0927. Calcd for $C_{12}H_{15}O_2$ (**10**): 191.1070. Found: 191.1055. MS (75 eV) *m/z* (relative intensity): 421 ($M^+ + 1$, 34%), 420 (M^+, base peak), 352 (24), 216 (44), 215 (13), 201 (94), 191 (63), 173 (66), 171 (12), 147 (75). UV λ_{max}^{EtOH} nm (log ε): 248 (3.58), 259 (3.55), 285 (3.50). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3480, 3300 (sh), 1620, 1600 (sh), 1500. ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.39 (6H, s, $C_{7'}$-CH_3 × 2), 1.67, 1.78 (each 3H, br s, $C_{11''}$-CH_3), 1.88 (2H, quintet, *J* = 8 Hz, C_2-H × 2), 2.61 (2H, t, *J* = 8 Hz, C_1-H × 2), 2.69 (2H, t, *J* = 8 Hz, C_3-H × 2), 3.44 (2H, br d, *J* = 7 Hz, $C_{9''}$-H × 2), 4.73 (2H, br s, OH × 2, disappeared on addition of D_2O), 5.12 (1H, br t, *J* = 7 Hz, $C_{10''}$-H), 5.27 (1H, dd, *J* = 1, 10.5 Hz, $C_{11'}$-H, *cis*), 5.33 (1H, dd, *J* = 1, 17.5 Hz, $C_{11'}$-H, *trans*), 5.76 (1H, br s, OH, disappeared on addition of D_2O), 6.16 (1H, dd, *J* = 10.5, 17.5 Hz, $C_{10'}$-H), 6.30 (1H, s, $C_{3'}$-H), 6.68 (1H, s, $C_{2''}$-H), 6.73 (1H, d, *J* = 2 Hz, $C_{7''}$-H), 6.94 (1H, s, $C_{6'}$-H), 7.55 (1H, d, *J* = 2 Hz, $C_{8''}$-H). The ^{13}C-NMR spectrum (100.4 MHz) is described in Table I.

Kazinol L Trimethyl Ether (2a)——A mixture of kazinol L (**2**, 12 mg), $(CH_3)_2SO_4$ (0.2 ml), and K_2CO_3 (5 g) in $(CH_3)_2CO$ (30 ml) was refluxed for 3 h and treated as usual. The reaction product was purified by preparative TLC (*n*-hexane : Et_2O = 5 : 1) to give a trimethyl ether (**2a**, 3 mg) as an oily substance. $FeCl_3$ test (negative). MS (75 eV) *m/z* (relative intensity): 463 ($M^+ + 1$, 37%), 462 (M^+, base peak), 230 (22), 219 (6), 215 (29). ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.42 (6H, s, $C_{7'}$-CH_3 × 2), 1.67, 1.78 (each 3H, br s, $C_{11''}$-CH_3), 1.85 (2H, m, C_2-H × 2), 2.64 (2H, t, *J* = 8 Hz, C_1-H × 2), 2.70 (2H, t, *J* = 8 Hz, C_3-H × 2), 3.45 (2H, br d, *J* = 6.5 Hz, $C_{9''}$-H × 2), 3.80, 3.81, 3.98 (each 3H, s, OCH_3), 4.91 (1H, dd, *J* = 1.5, 10 Hz, $C_{11'}$-H, *cis*), 4.92 (1H, dd, *J* = 1.5, 18 Hz, $C_{11'}$-H, *trans*), 5.13 (1H, br t, *J* = 6.5 Hz, $C_{10''}$-H), 6.17 (1H, dd, *J* = 10, 18 Hz, $C_{10'}$-H), 6.45 (1H, s, $C_{3'}$-H), 6.63 (1H, s, $C_{2''}$-H), 6.71 (1H, d, *J* = 2 Hz, $C_{7''}$-H), 7.01 (1H, s, $C_{6'}$-H), 7.56 (1H, d, *J* = 2 Hz, $C_{8''}$-H). The ^{13}C-NMR data (67.8 MHz) are summarized in Table I.

Kazinol M (3)——Compound **3** was obtained as an oily substance. $FeCl_3$ test (brown, coloration was weak and slowly), Gibbs test (positive), Na_2MoO_4 test (negative). High-resolution MS: Calcd for $C_{25}H_{30}O_4$ (M^+, *m/z*): 394.2141. Found: 394.2135. Calcd for $C_{16}H_{19}O_2$ (**14**): 243.1384. Found: 243.1390. Calcd for $C_7H_7O_2$ (**15**): 123.0445.

Found: 123.0445. MS (75 eV) m/z (relative intensity): 395 ($M^+ + 1$, 33%), 394 (M^+, 89), 379 (base peak), 243 (22), 215 (39), 197 (15), 189 (23), 123 (45). UV λ_{max}^{EtOH} nm (log ε): 228 (4.52), 266 (infl. 3.87), 277 (4.06), 286 (sh 4.00), 325 (3.21). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3550, 3380 (br), 1620, 1600, 1510. ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.41 (6H, s, $C_{9''}$-$CH_3 \times 2$), 1.65, 1.70 (each 3H, br s, $C_{14''}$-CH_3), 1.78 (2H, m, C_2-$H \times 2$), 2.50 (2H, t, $J=8$ Hz, C_3-$H \times 2$), 2.54 (2H, t, $J=7.5$ Hz, C_1-$H \times 2$), 3.23 (2H, br d, $J=5.5$ Hz, $C_{12''}$-$H \times 2$), 4.95 (1H, br t, $J=5.5$ Hz, $C_{13''}$-H), 5.4—5.8 (3H, br, disappeared on addition of D_2O), 5.62 (1H, d, $J=10$ Hz, $C_{8''}$-H), 6.30 (1H, d, $J=2$ Hz, $C_{3'}$-H), 6.33 (1H, dd, $J=2$, 8 Hz, $C_{5'}$-H), 6.48 (1H, d, $J=10$ Hz, $C_{7''}$-H), 6.65 (1H, s, $C_{2''}$-H), 6.90 (1H, d, $J=8$ Hz, $C_{6'}$-H). The ^{13}C-NMR data (100.4 MHz) are summarized in Table I.

Kazinol M Trimethyl Ether (3a)——A mixture of kazinol M (**3**, 15 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 reaction product was purified by preparative TLC ($CHCl_3$ only) to give a trimethyl ether (**3a**, 10 mg) as an oily substance. $FeCl_3$ test: negative. MS (75 eV) m/z (relative intensity): 437 ($M^+ + 1$, 23%), 436 (M^+, 71), 422 (36), 421 (base peak), 257 (11), 151 (23). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1620, 1590, 1500. ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.44 (6H, s, $C_{7'}$-$CH_3 \times 2$), 1.66, 1.71 (each 3H, br s, $C_{14''}$-CH_3), 1.80 (2H, m, C_2-$H \times 2$), 2.55 (2H, t, $J=8$ Hz, C_3-$H \times 2$), 2.61 (2H, t, $J=7.5$ Hz, C_1-$H \times 2$), 3.26 (2H, br d, $J=5.5$ Hz, $C_{12''}$-$H \times 2$), 3.78 (6H, s, $OCH_3 \times 2$), 3.82 (3H, s, OCH_3), 4.98 (1H, br t, $J=5.5$ Hz, $C_{13''}$-H), 5.63 (1H, d, $J=10$ Hz, $C_{8''}$-H), 6.41 (1H, dd, $J=2$, 8 Hz, $C_{5'}$-H), 6.44 (1H, d, $J=2$ Hz, $C_{3'}$-H), 6.48 (1H, d, $J=10$ Hz, $C_{7''}$-H), 6.61 (1H, s, $C_{2''}$-H), 7.02 (1H, d, $J=8$ Hz, $C_{6'}$-H). The ^{13}C-NMR data (100.4 MHz) are summarized in Table I.

Kazinol N (4)——Compound **4** was obtained as an oily substance. $FeCl_3$ test (brown, coloration was weak and slowly), Na_2MoO_4 test (negative). High-resolution MS: Calcd for $C_{26}H_{32}O_4$ (M^+, m/z): 408.2298. Found: 408.2294. Calcd for $C_{16}H_{19}O_2$ (**14**): 243.1384. Found: 243.1373. Calcd for $C_8H_9O_2$ (**16**): 137.0602. Found: 137.0593. MS (75 eV) m/z (relative intensity): 409 ($M^+ + 1$, 23%), 408 (M^+, 69), 393 (base peak), 243 (12), 215 (21), 189 (17), 173 (6), 137 (36). UV λ_{max}^{EtOH} nm (log ε): 231 (4.47), 266 (infl. 3.84), 276 (4.04), 286 (sh 3.97), 325 (3.21). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3550, 3360 (br), 1620, 1600, 1505. ^1H-NMR ($CDCl_3$, 400 MHz) δ: 1.41 (6H, s, $C_{9''}$-$CH_3 \times 2$), 1.66, 1.71 (each 3H, br s, $C_{14''}$-CH_3), 1.77 (2H, m, C_2-$H \times 2$), 2.50 (2H, t, $J=8$ Hz, C_3-$H \times 2$), 2.57 (2H, t, $J=7.5$ Hz, C_1-$H \times 2$), 3.24 (2H, br d, $J=6$ Hz, $C_{12''}$-$H \times 2$), 3.75 (3H, s, OCH_3), 4.96 (1H, br t, $J=6$ Hz, $C_{13''}$-H), 5.26, 5.38 (each 1H, br s, OH, disappeared on addition of D_2O), 5.62 (1H, d, $J=10$ Hz, $C_{8''}$-H), 6.32 (1H, dd, $J=2.5$, 8 Hz, $C_{5'}$-H), 6.38 (1H, d, $J=2.5$ Hz, $C_{3'}$-H), 6.49 (1H, d, $J=10$ Hz, $C_{7''}$-H), 6.66 (1H, s, $C_{2''}$-H), 6.93 (1H, d, $J=8$ Hz, $C_{6'}$-H). The ^{13}C-NMR data (100.4 MHz) are summarized in Table I.

Methylation of Kazinol N (4) [Formation of Kazinol M Trimethyl Ether (3a)]——A mixture of kazinol N (**4**, 20 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 reaction product was purified by preparative TLC (benzene : $CHCl_3 = 1 : 1$) to give a dimethyl ether (15 mg) as an oily substance. $FeCl_3$ test (negative). The dimethyl ether was identical with kazinol M trimethyl ether (**3a**) on the basis of TLC, IR and ^1H-NMR spectral comparisons.

Treatment of Kazinol J (1) with DDQ [Formation of Kazinol N (4) from 1]——A mixture of **1** (100 mg) and DDQ (60 mg) in dry benzene (30 ml) was kept at room temperature for 3 h. The reaction product was purified by preparative TLC (n-hexane : $(CH_3)_2CO = 2 : 1$; Et_2O : n-hexane $= 2 : 1$) to give **4** (1 mg). Compound **4** thus obtained was identical with kazinol N on the basis of MS and ^1H-NMR spectral comparisons, and TLC.

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References and Notes

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