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Studies on *Xanthoxylum* spp. II.[1] Constituents of the Bark of *Xanthoxylum piperitum* DC.[2]

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The stem bark of *Xanthoxylum piperitum* DC. was phytochemically examined and five new lignans, *viz.*, xanthoxylol (**3**), piperitol (**5**), their γ,γ-dimethylallyl ethers (**6,7**) and sanshodiol (**8**) were isolated besides *l*-asarinin (**1**) and *l*-sesamin (**2**) and their structures were determined.

Phytosterol, γ-fagarine, skimmianine, syringaldehyde, piperonylic acid, menisperine, laurifoline and magnoflorine were also isolated from the same source.

In the preceding paper[1] dealing with the examination of constituents of the root of *Xanthoxylum piperitum* DC., the authors reported the isolation of phytosterol, aesculetin dimethyl ether, methyl 2,4-dimethoxy-5-hydroxycinnamate, skimmianine, γ-fagarine, menisperine, magnoflorine, laurifoline and *l*-sesamin. As the continuation of our work on *Xanthoxylum piperitum* DC., we have investigated the constituents of the bark and isolated five new lignans (I—V) besides *l*-asarinin, *l*-sesamin, phytosterol, syringaldehyde, piperonylic acid and the same alkaloids isolated from the root. This paper concerns the isolation and the structures of the new lignans.[4]

The air-dried bark was extracted with hot methanol and the methanol extractives were successively extracted with hot hexane (Fr. A), chloroform (Fr. B) and then with water (Fr. C). Repeated column chromatography of Fr. A on silica gel furnished *l*-asarinin, phytosterol, *l*-sesamin and two new compounds (I and II). Fr. B was fractionated to the basic and acidic fractions. Both fractions were respectively chromatographed on silica gel and were isolated γ-fagarine and skimmianine from the basic fraction and three new compounds (III—V) together with syringaldehyde and piperonylic acid from the acidic fraction. From Fr. C, chlorides of three quarternary bases were obtained through the base-reineckate procedure followed by chromatographic purification. Bases were converted to the crystalline salts and were identified with menisperine, laurifoline and magnoflorine, respectively.

l-Asarinin and *l*-sesamin showed on thin-layer chromatography (TLC) plates the dark green color immediately after spraying 10% sulfuric acid and heating, and then the color turned to reddish violet. I—V gave the same color reaction, which suggested that all of them are compounds closely related to *l*-asarinin and *l*-sesamin.

III, $C_{20}H_{20}O_6$, colorless needles, mp 140—142°, $[\alpha]_D$ −117°, stained reddish brown by diazotized benzidine reagent and showed the infrared (IR) absorption of hydroxyl group at 3550 cm^{-1}. It gave a monoacetate on acetylation, and a monoethyl ether was obtained when

1) Part I: F. Abe, M. Furukawa, G. Nonaka, H. Okabe, and I. Nishioka, *Yakugaku Zasshi*, **93**, 624 (1973).
2) A part of this work was reported at the 93rd Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1973. Communication: F. Abe, S. Yahara, G. Nonaka, H. Okabe, and I. Nishioka, *Chem. Pharm. Bull.* (Tokyo), **21**, 1617 (1973).
3) Location: *Katakasu, Higashi-ku, Fukuoka*; *a*) Present address: *Faculty of Pharmaceutical Sciences, Fukuoka University, Nanakuma, Nishi-ku, Fukuoka.*
4) The isolation of these lignans from the bark urged us to re-examine the root constituents and the thin-layer chromatographic examination has revealed the presence of all the above-mentioned lignans but V in the 5% acetic acid insoluble fraction of the methanol extractives. (*cf.* Part 1).

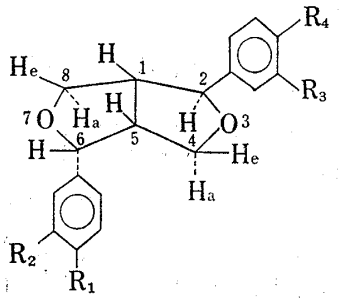
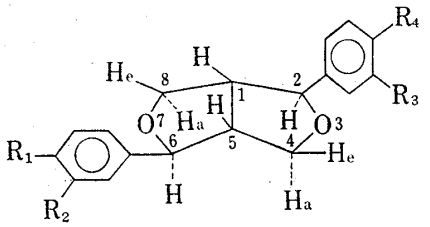
Table I. NMR Spectral Data[a,b]

	C_2–H	C_6–H	C_1–H	C_5–H	C_4–H	C_8–H
l-Asarinin	4.81 d (4.5)	4.39 d (6.7)	2.60—3.05 m	3.05—3.50 m (C_5–H, C_4–Ha)	3.50—4.21 m (C_4–He, C_8–Hae)	
l-Sesamin	4.71 d (4.5)		2.85—3.20 m (C_1–H, C_5–H)		3.85 dd (9.0, 3.5, $C_{4,8}$–Ha) 4.25 dd (9.0, 6.5, $C_{4,8}$–He)	
I	4.82 d (4.5)	4.41 d (6.7)	2.65—3.10 m	3.10—3.50 m (C_5–H, C_4–Ha)	3.50—4.25 m (C_4–He, C_8–Hae)	
II	4.72 d (4.0)		2.90—3.20 m C_1–H, C_5–H)		3.85 dd (9.0, 3.5, $C_{4,8}$–Ha) 4.25 dd (9.0, 6.5, $C_{4,8}$–He)	
III (Xanthoxylol)	4.82 d (4.5)	4.40 d (6.7)	2.70—3.10 m	3.10—3.50 m (C_5–H, C_4–Ha)	3.50—4.25 m (C_4–He, C_8–Hae)	
Acetate of III	4.82 d (4.5)	4.47 d (6.7)	2.85—3.10 m	3.10—3.50 m (C_5–H, C_4–Ha)	3.50—4.30 m (C_4–He, C_8–Hae)	
IV (Piperitol)	4.72 d (4.5)		2.85—3.25 m (C_1–H, C_5–H)		3.85 dd (9.0, 3.5, $C_{4,8}$–Ha) 4.26 dd (9.0, 6.5, $C_{4,8}$–He)	
Acetate of IV	4.71 d (4.5)	4.78 d (4.5)	2.85—3.20 m (C_1–H, C_5–H)		3.86 dd (9.0, 3.5, $C_{4,8}$–Ha) 4.26 dd (9.0, 6.5, $C_{4,8}$–He)	

	Ar–H	$-O\diagdown CH_2 \diagup O-$	$-OCH_3$	–OH	–OAc	$-OCH_2CH=C(CH_3)_2$ (c b a)
l-Asarinin	6.75—6.90 m	5.95 s				
l-Sesamin	6.75—6.88 m	5.93 s				
I	6.75—6.95 m	5.95 s	3.88 s			1.74 br.s (Ha) 5.52 br.t (7.0, Hb) 4.56 d (7.0, Hc)
II	6.75—6.95 m	5.92 s	3.88 s			1.75 br.s (Ha) 5.52 br.t (7.0, Hb) 4.56 d (7.0, Hc)
III (Xanthoxylol)	6.76—6.93 m	5.95 s	3.90 s	5.65 br.s		
Acetate of III	6.77—7.05 m	5.95 s	3.85 s		2.31 s	
IV (Piperitol)	6.76—7.93 m	5.96 s	3.90 s	5.75 br.s		
Acetate of IV	6.77—7.05 m	5.93 s	3.83 s		2.30 s	

a) Run at 60 MHz. Chemical shifts are in parts per million and numbers in parentheses are coupling constants in Hz.
b) Reports by Taylor, *et al.*[5] and McCarthy, *et al.*[c] were referred for assignment of signals.
c) C.H. Ludwig, B.J. Nist and J.L. McCarthy, *J. Amer. Chem. Soc.*, **86**, 1186 (1964)

treated with diazoethane. The nuclear magnetic resonance (NMR) spectrum (Table I) revealed the presence of each one methylenedioxy and methoxyl groups and six aromatic protons, and the striking similarity of the spectrum to that of *l*-asarinin, although the signal of one methylenedioxy group of *l*-asarinin is replaced by those of methoxyl and hydroxyl groups, indicated that III has the same stereostructure as that of *l*-asarinin (**1**) and it differs from

1 *l*-asarinin:	$R_1R_2=R_3R_4$; $-OCH_2O-$	2 *l*-sesamin:	$R_1R_2=R_3R_4$; $-OCH_2O-$
3 III (xanthoxylol):	R_1; $-OH$, R_2; $-OCH_3$, R_3R_4; $-OCH_2O-$	5 IV (piperitol):	R_1; ; $-OH$, R_2; $-OCH_3$, R_3R_4; $-OCH_2O-$
4 pluviatilol:	R_1R_2; $-OCH_2O-$, R_3; $-OCH_3$; R_4; $-OH$	7 II:	R_1; $-OCH_2CH=C(CH_3)_2$, R_2; $-OCH_3$, R_3R_4; $-OCH_2O-$
6 I:	R_1; $-OCH_2CH=C(CH_3)_2$, R_2; $-OCH_3$, R_3R_4; $-OCH_2O-$		

Chart 1

the latter only in the substituents on the aromatic ring. When the ethyl ether was oxidized with potassium permanganate, it afforded piperonylic acid and vanillic acid ethyl ether. Therefore, the alternative structures (**3**) and (**4**) may be proposed for III, the latter of which was assigned by Taylor, *et al.*[5] to pluviatilol, a phenolic lignan isolated from *Xanthoxylum pluviatile*. The IR spectrum of III was not quite identical with that of pluviatilol and the methyl ether (mp 123—125°) showed depression of the melting point on admixture with pluviatilol methyl ether (mp 134—135°). The latter structure (**4**) was therefore ruled out and the former (**3**) remained as the possible structure of III. In the NMR spectrum of its acetate, the benzylic methine proton (C_6–H) of III which resonated as a doublet at 4.40 ppm (J=6.7 Hz) was shifted by 4.2 Hz downfield, while the other (C_2–H, 4.82 ppm, doublet, J=4.5 Hz) stayed at the same position. On this basis,[6] III is shown to have the *quasi*-axial 3-methoxy-4-hydroxyphenyl group linked to the 6-carbon atom, and the *quasi*-equatorial 3,4-methylenedioxyphenyl group at the 2-carbon. Consequently the structure of III is defined as **3**.

IV, $C_{20}H_{20}O_6$, colorless syrup, $[\alpha]_D$ −66.3°, has the same functional groups with those of III, and its very similar NMR spectrum to that of *l*-sesamin indicated that IV is the sesamin-type isomer of III. The NMR signal of one benzylic methine proton out of the two (4.72 ppm, doublet, J=4.5 Hz) was moved downfield to 4.78 ppm when IV was acetylated, and the ethyl ether gave piperonylic acid and vanillic acid ethyl ether on permanganate oxidation. Hence, IV was assigned the structure (**5**).

I, $C_{25}H_{28}O_6$, colorless oil, $[\alpha]_D$ −86.5°, showed on IR spectrum the presence of double bond at 1590 cm^{-1} and *gem.* dimethyl group at 1390 cm^{-1}. Its NMR spectrum was almost superimposable on that of III except for the additional signals of *gem.* dimethyl protons (1.74 ppm, broadened singlet) and one vinyl proton (5.52 ppm, broadened triplet, J=7.0 Hz) which couples with the oxygenated methylene protons (4.56 ppm, doublet, J=7.0 Hz). The mass spectrum showed peaks at *m/e* 69 $[(CH_3)_2C{=}CH{-}CH_2]^+$, 356 $[M-69+H]^+$ and 424 $[M]^+$.

5) J.E.T. Corrie, G.H. Green, E. Ritchie, and W.C. Taylor, *Aust. J. Chem.*, **23**, 133 (1970).

6) In hope that the similar phenomenon might be observed in other phenols, the spectra of syringaldehyde and some methyl hydroxycinnamates were examined. The aldehydic proton of syringaldehyde was shifted downfield by 5.4 Hz on acetylation of *p*-hydroxyl group. In the cases of *p*-hydroxycinnamates, the effect was relayed by the double bond to the α-carbon atom, *i.e.*, the proton (H_α) on the α-carbon atom was shifted downfield by 5.4 Hz, while the proton (H_β) on the β-carbon was very little affected. On the other hand, H_α and H_β of *o*-hydroxycinnamates were shifted upfield by *ca.* 11 Hz and 16 Hz, respectively. H_α of *m*-hydroxycinnamates showed no shift, whereas H_β was moved upfild by 2—3 Hz. These upfield shifts are probably due to the magnetic anisotropy of the acetyl group in the vicinity. These findings provide further support on the orientation of the hydroxyl group in III.

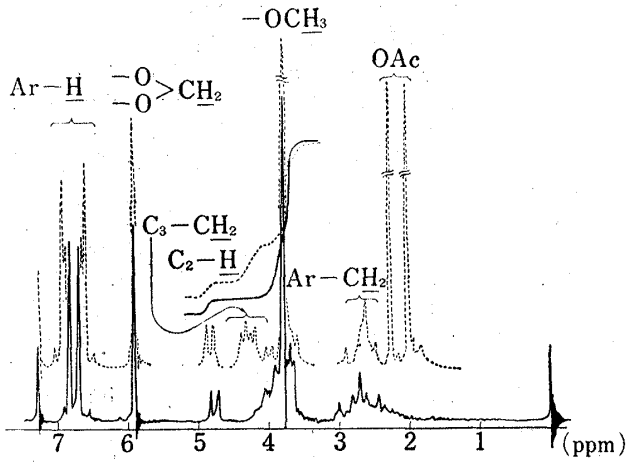


Fig. 1. NMR Spectra of Sanshodiol (V) (——) and Its Acetate (·····)

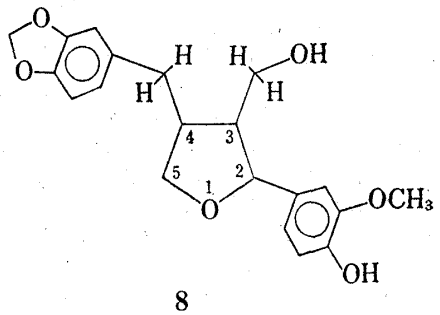


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Chart 2

These spectral data, coupled with the molecular formula, strongly suggested that I is the γ,γ-dimethylallyl ether (**6**) of III, and actually I was provided when III was treated with isoprene monohydrobromide.

II, $C_{25}H_{28}O_6$, colorless needles, mp 58—59°, $[\alpha]_D$ −45.7°, gave almost analogous mass and IR spectral data to those of I, but unlike I, it exhibited the NMR spectrum closely related to that of IV. Thus, II was assumed as the γ,γ-dimethylallyl ether (**7**) of IV. The synthetic γ,γ-dimethylallyl etherof IV was identical with II in all respects.

V, $C_{20}H_{22}O_6$, colorless fine needles, mp 140—141°, $[\alpha]_D$ −14.4°, is sensitive to diazotized benzidine reagent and showed the IR absorption of hydroxyl groups at 3400 and 3500 cm^{-1}. The NMR spectrum (Fig. 1) revealed the presence of each one methylenedioxy and methoxyl groups, six aromatic and one benzylic methine protons. When V was acetylated, it gave a diacetate (Mass: $[M]^+$ 442). In the NMR spectrum of the acetate, the benzylic methine proton signal (4.78 ppm, doublet, J=6.0 Hz) was shifted by *ca.* 4 Hz downfield and signals of the two oxygenated methylene protons were moved from 3.50—4.25 ppm to 4.10—4.40 ppm. These NMR data showed that V has a hydroxymethyl group and a methoxyhydroxyphenyl group which links to the 2-carbon atom of the hydrofuran ring. Although the small quantity of the material precluded the oxidative degradation to settle the location of the functional groups on the aromatic rings, they may safely be placed at 3,4-positions because V gave almost the same NMR signals of aromatic protons as those of other aforesaid lignans, and also this orientation seems reliable from the biogenetic grounds. It was assumed that V is a dihydro derivative of III or IV having a 3,4-methylenedioxybenzyl residue. This assumption was well supported by mass spectra of both V and its acetate which showed the fragment ion peak (*m/e* 135) attributable to the methylenedioxybenzyl ion as the base peak. Therefore, the plane structure (**8**) is proposed for V. The stereostructure could not be examined because of the poor yield of V.

The above-mentioned lignans are new and the authors propose the names xanthoxylol (**3**), piperitol (**5**) and sanshodiol (**8**) for respective III, IV and V. γ,γ-Dimethylallyl ethers (**6**, **7**) of xanthoxylol and piperitol are the first naturally occurring lignans having prenyl ether.

Experimental[7]

Extraction and Fractionation——The bark (40 kg) of *Xanthoxylum piperitum* collected in Kumamoto

7) Melting points were determined on a Yanagimoto micro melting point apparatus, and are uncorrected. NMR spectra were taken at 60 MHz on a JEOL-JNM-C-60 H spectrometer in $CDCl_3$ using Me_4Si as internal reference and chemical shifts are shown in δ-scale (s: singlet, d: doublet, t: triplet, m: multiplet, br: broadened). Mass spectra were obtained with a JEOL-JNM-01SG spectrometer provided with a glass inlet system. Conditions for measurement are written in the order: ionizing volt., ionizing current, sample temp., chamber temp., accel. volt. and ion multi. voltage. Specific rotations were measured with a JASCO automatic polarimeter DIP-SL, and IR spectra were obtained with Nippon Bunko DS-301 and DS-701G spectrometers, and UV spectra with a Shimazu SV-50A spectrophotometer. TLC was conducted on Kieselgel G nach Stahl. In column chromatography, Kieselgel (70—200 mesh) (E. Merck) was employed.

Prefecture in June and July 1971 was crushed and extracted with hot MeOH. MeOH was evaporated off *in vacuo* to give a dark brown syrup (*ca.* 4 kg). The MeOH extractives were redissolved in MeOH and Celite 545 was added to the solution, and then the solvent was evaporated off to give a dry powder. The powder was repeatedly extracted with hot hexane. Hexane was evaporated *in vacuo* to give an oily residue (Fr. A) (960 g). The remaining powder was packed in a glass tube and was percolated successively with $CHCl_3$ and water. $CHCl_3$ percolate was concentrated *in vacuo* to give a brown resinous residue (Fr. B) (1200 g). The H_2O percolate was used for isolation of quarternary bases without concentration.

Fractionation of Fr. A——Fr. A was subjected to column chromatography over silica gel using the hexane–AcOEt mixture. Every fraction was monitored by TLC and fractions with the same chromatogram were combined. Fr. A was divided to five fractions (Fr. A-1—5). Fr. A-2[hexane–AcOEt (9: 1) eluate] was rechromatographed on silica gel eluted with benzene–AcOEt (97: 3) to give *l*-asarinin (14.4 g) and phytosterol (*ca.* 10 g). Fr. A-3 [hexane–AcOEt (9: 1) eluate] was pure *l*-sesamin (72 g). Fr. A-4 [hexane–AcOEt (4: 1) eluate] was repeatedly chromatographed on silica gel using benzene–AcOEt (19: 1), hexane–ether (17: 3) and benzene–ether (19: 1) and thin-layer chromatographically pure xanthoxylol γ,γ-dimethylallyl ether (I) (2.7 g) and piperitol γ,γ-dimethylallyl ether (II) (4.1 g) were obtained.

l-Asarinin: Colorless needles from $CHCl_3$–MeOH, mp 122—124°, $[\alpha]_D^{20}$ −122° (c=2.10, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 237 (3.99), 288 (3.96). Mass Spectrum (75 eV, 200 μA, 90°, 181°, 6.2 kV, 1.0 kV): $[M]^+$ *m/e* 354. *Anal.* Calcd. for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.72; H, 5.22. Phytosterol (a mixture of campe- and β-sitosterols): Colorless prisms from MeOH–acetone, mp 142—143°. GLC (1.5% SE-30, 2.5 m×4 mmϕ, column temperature 248°): t_R 4.2, 5.2 min (campesterol: t_R 4.2 min; β-sitosterol: t_R 5.2 min).

l-Sesamin: Colorless prisms from MeOH, mp 124—126°, $[\alpha]_D^{19}$ −68.6° (c=0.53, $CHCl_3$). It showed a quite identical IR spectrum with that of *l*-sesamin isolated from the root and showed no depression of the melting point on admixture. Xanthoxylol γ,γ-dimethylallyl ether (I): Colorless oil, $[\alpha]_D^{19}$ −86.5° (c=4.08, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 234 (4.28), 284 (3.97), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1610, 1590, 1390. Mass Spectrum (75 eV, 200 μA, 80°, 129°, 6.1 kV, 1.5 kV): $[M]^+$ Calcd. for $C_{25}H_{28}O_6$; 424.189. Found: 424.189. *m/e* 356, 151, 149, 86, 84, 69.

Piperitol γ,γ-Dimethylallyl Ether (II): Colorless needles from MeOH, mp 58—59°, $[\alpha]_D^{20}$ −45.7° (c= 5.38, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 234 (4.26), 2.84 (3.95), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1610, 1590, 1380. Mass Spectrum (75 eV, 100 μA, 95°, 173°, 6.1 kV, 1.5 kV): $[M]^+$ Calcd. for $C_{25}H_{28}O_6$: 424.189. Found: 424.190. *m/e* 356, 151, 149, 69.

Fractionation of Fr. B——Fr. B was dissolved in $CHCl_3$ and extracted with 5% HCl solution. The acidic solution was made alkaline with dil. NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried over Na_2SO_4 and then the solvent was evaporated off to give a resinous residue (Fr. B-1). Fr. B-1 was repeatedly chromatographed over silica gel using $CHCl_3$–MeOH mixture and hexane–AcOEt to give γ-fagarine (160 mg) and skimmianine (310 mg). The $CHCl_3$ solution after extraction with 5% HCl was then extracted with 5% NaOH. The alkaline solution was acidified with dil. HCl and was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried over Na_2SO_4 and concentrated *in vacuo* to give a resinous residue (Fr. B-2). Fr. B-2 was repeatedly chromatographed on silica gel using $CHCl_3$–MeOH and hexane–AcOEt to give thin-layer chromatographically homogeneous xanthoxylol (1.8 g), piperitol (2.1 g), syringaldehyde (30 mg), sanshodiol (V) (28 mg) and piperonylic acid (25 mg).

γ-Fagarine: Colorless prisms from MeOH, mp 140—142°. IR spectrum was quite identical with that of γ-fagarine isolated from the root. It showed no depression of the melting point on admixture with the authentic sample.

Skimmianine: Pale yellow prisms from MeOH, mp 178—180°. IR spectrum was superimposable on that of skimmianine and no depression of the melting point was observed on admixture with skimmianine from the root.

Xanthoxylol (III): Colorless pillars from hexane–benzene, mp 140—142°. $[\alpha]_D^{16}$ −117° (c=0.50, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 233 (4.06), 285 (3.82). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1610. Mass Spectrum (75 eV, 200 μA, 81°, 184°, 6.3 kV, 1.5 kV): $[M]^+$ Calcd. for $C_{20}H_{20}O_6$: 356.126. Found: 356.124. *m/e* 325, 205, 150, 149. Acetate: Colorless oil, $[\alpha]_D^{23}$ −83.2° (c=0.48, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 281 (3.94). Mass Spectrum: $[M]^+$ Calcd. for $C_{22}H_{22}O_7$: 398.137. Found: 398.134. Methyl ether: III was treated with diazoemethane etherate for overnight; colorless prisms, mp 123—125°. Mass Spectrum: $[M]^+$ Calcd. for $C_{21}H_{22}O_6$: 370.142. Found: 370.143. NMR: 3.88 (3H, s, $-OCH_3$), 3.90 (3H, s, $-OCH_3$), 4.42 (1H, d, J=6.5 Hz, C_6-H), 4.83 (1H, d, J=4.7 Hz, C_2-H), 5.95 (2H, s, $-OCH_2O-$), 6.76—6.95 (6H, aromatic H). Ethyl ether: III was treated with diazoethane; colorless oil. Mass Spectrum: $[M]^+$ 384. NMR: 1.46 (3H, t, J=7.0 Hz, $-OCH_2\underline{C}H_3$), 3.90 (3H, s, $-OCH_3$), 3.97 (2H, q, J=7.0 Hz, $-O\underline{C}H_2CH_3$), 4.42 (1H, d, J=6.7 Hz, C_6-H), 4.84 (1H, d, J=3.7 Hz, C_2-H), 5.96 (2H, s, $-OCH_2O-$), 6.81—6.98 (6H, aromatic H).

Piperitol (IV): Colorless oil, $[\alpha]_D^{21}$ −66.3° (c=2.50, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 233 (4.11), 285 (3.87). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1610. Mass Spectrum (75 eV, 200 μA, 95°, 175°, 6.4 kV, 1.3 kV): $[M]^+$ Calcd. for $C_{20}H_{20}O_6$: 356.126, Found: 356.127. Acetate: Colorless prisms from hexane–AcOEt. mp 115—116°, $[\alpha]_D^{23}$ −56.0° (c=1.75, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 281 (4.09). Mass Spectrum: $[M]^+$ Calcd. for $C_{22}H_{22}O_7$: 398.137. Found: 398.136. Ethyl ether: Colorless oil, $[\alpha]_D^{16}$ −54.3° (c=0.29, $CHCl_3$). UV λ_{max}^{MeOH} nm (log ε): 234 (4.26), 284 (3.95). Mass Spectrum: $[M]^+$ Calcd. for $C_{22}H_{24}O_6$: 384.157. Found: 384.155. NMR:

1.45 (3H, t, J=7.5 Hz, $-OCH_2\underline{CH_3}$), 2.90—3.25 (2H, m, $C_{1,5}$-H), 3.86 (2H, d,d., J=9.0, 3.7 Hz, $C_{4,8}$-Ha), 3.89 (3H, s, $-OCH_3$), 4.09 (2H, q, J=7.5 Hz, $-O\underline{CH_2}CH_3$), 4.26 (2H, d.d., J=9.0, 7.5 Hz, $C_{4,8}$-He), 4.72 (2H, d, J=4.0 Hz, $C_{2,6}$-Ha, 5.94 (2H, s, $-OCH_2O-$), 6.75—6.94 (6H, aromatic H).

Syringaldehyde: Pale yellow needles from MeOH, mp 113—114.5°. UV λ_{max}^{MeOH} nm (log ε): 231 (4.31), 310 (4.20). IR ν_{max}^{KBr} cm^{-1}: 3300, 1670. *Anal.* Calcd. for $C_9H_{10}O_4$: C, 59.33; H, 5.53. Found: C, 59.38; H, 5.64. NMR: 3.99 (6H,s,$-OCH_3\times2$), 6.30 (1H, broadened s, -OH), 7.16 (2H, s, aromatic H), 9.79 (1H, s, -CHO).

Sanshodiol (V): Colorless needles from hexane–AcOEt, mp 140—141°, $[\alpha]_D^{16}$ −14.4° (c=1.0, $CHCl_3$), UV λ_{max}^{MeOH} nm (log ε): 233 (4.19), 286 (3.95). IR ν_{max}^{KBr} cm^{-1}: 3400, 3500. Mass Spectrum (75 eV, 200μA, 135°, 189°, 6.3 kV, 1.1 kV): $[M]^+$ Calcd. for $C_{20}H_{22}O_6$: 358.142. Found: 358.141. m/e 194, 135. NMR: 1.94 (1H, broadened s, $-CH_2O\underline{H}$), 2.20—3.00 (4H, m, C_4-CH_2, $C_{3,4}$-H) 3.50—4.25 (4H, m, C_3-CH_2, C_5-H_2), 3.86 (3H, s, $-OCH_3$), 4.78 (1H, d, J=6.0 Hz, C_2-H), 5.93 (2H, s, $-OCH_2O-$), 6.70 (3H, aromatic H), 6.84 (3H, aromatic H). Acetate: Colorless oil. UV λ_{max}^{MeOH} nm (log ε): 281 (4.06). Mass Spectrum: m/e 442, 400, 340, 219, 188, 151, 135. NMR: 2.05 (3H, s, $-COCH_3$), 2.30 (3H, s, $-COCH_3$), 2.30—2.90 (4H, m, C_4-CH_2, $C_{3,4}$-H), 3.50—4.10 (2H, m, C_5-H), 4.10—4.40 (2H, m, C_3-CH_2), 4.84 (1H. d, J=4.5 Hz, C_2-H), 5.92 (2H, s, $-OCH_2O-$), 6.69 (3H, aromatic H), 6.91 (3H, aromatic H).

Piperonylic Acid: Pale yellow needles from $CHCl_3$–MeOH, mp 208—216° (decomp.). UV λ_{max}^{MeOH} nm (log ε): 260 (3.76), 296 (3.70). IR ν_{max}^{KBr} cm^{-1}: 1670, 1620, 1605. Mass Spectrum: m/e 166 $[M]^+$. NMR: 6.15 (2H, s, $-OCH_2O-$), 7.01 (1H, d, J=8.0 Hz, aromatic H), 7.39 (1H, d, J=1.5 Hz, aromatic H), 7.58 (1H, d.d., J=1.5, 8.0 Hz, aromatic H), 12.75 (1H, broadened s, -COOH).

Isolation of Quarternary Bases from Fr. C——Fr. C was acidified by adding conc. HCl, the saturated NH_4-reineckate solution was added and the precipitates were filtered and extracted with acetone. The acetone extract was passed through an alumina column and the eluted base-reineckates were converted to chlorides by the conventional method. Chlorides were separated by silica gel column chromatography eluted with $CHCl_3$–MeOH–H_2O (7 : 3 : 0.05) to thin-layer chromatographically homogeneous state. Every quarternary base chloride was converted into the crystalline salt according to the usual methods.

Menisperine: styphnate; yellow needles from MeOH, mp 207—209°.

Laurifoline: picrate; yellow needles from MeOH, mp 218—220°.

Magnoflorine: styphnate; yellow needles from MeOH–acetone, mp 213—220° (decomp.).

All the above-mentioned quarternary base salts showed the identical IR spectra with those of authentic specimens.

γ,γ-Dimethylallyl Ethers of III and IV——To a solution of III (230 mg) in acetone (8 ml) were added anhydrous potassium carbonate (180 mg) and excess isoprene monohydrobromide (bp 57—58°/38 mmHg). The mixture was refluxed for 7 hr. After cooling the mixture, the precipitates were filtered off and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography to afford colorless oil (250 mg). Mass Spectrum: $[M]^+$ Calcd. for $C_{25}H_{28}O_6$: 424.189. Found: 424.189. Specific rotation and UV, IR and NMR spectra were identical with those of I. The same procedure on IV (313 mg) gave the corresponding γ,γ-dimethylallyl ether (370 mg): colorless needles, mp 59—60°, Mass Spectrum: $[M]^+$ Calcd. for $C_{25}H_{28}O_6$; 424.189. Found: 424.185. Specific rotation and UV, IR and NMR spectra were identical with those of II.

Permanganate Oxidation of Ethyl Ethers of III and IV——To the warm (80—85°) aqueous acetone solution of IV ethyl ether (215 mg), 5% $KMnO_4$ in aqueous acetone (60 ml) was added dropwise over a period of 2 hr, then refluxed for 1 hr, and left stand at room temperature overnight. The excess $KMnO_4$ was consumed with MeOH and precipitated MnO_2 was filtered off. Acetone was distilled and the remaining water solution was washed with $CHCl_3$. The aqueous solution was acidified with dil. H_2SO_4 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed, dried and concentrated. The residue was methylated with diazomethane etherate and checked by GLC (1.5% SE-52, 2.25 m×4 mmϕ, temperature 170°) to give two peaks at t_R 1.3 and 2.6 min (methyl piperonylate: t_R 1.3 min, methyl vanillate ethyl ether: t_R 2.6 min). Methyl esters were separated by column chromatography monitoring by GLC to give methyl piperonylate: mp 50—52° and methyl vanillate ethyl ether: mp 79—81°. They showed no depression of the melting points on admixture with authentic samples. The same experiment on III ethyl ether gave the same results.

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