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LIGNANS IN FLOWER BUDS OF *MAGNOLIA FARGESII*

H. KAKISAWA
Department of Chemistry, Tokyo Kyoiku University, Otsuka, Tokyo, Japan

and

Y. P. CHEN and H. Y. HSÜ
Bristol Research Institute of Taiwan, Taipei, Taiwan

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Key Word Index—*Magnolia fargesii;* Magnoliaceae; lignans; magnolin; fargesin; di-*O*-methylpinoresinol; B-di-*O*-methyl lirioresinol.

Abstract—Four lignans were isolated from the flower buds of *Magnolia fargesii* Cheng, two of which were known lignans, pinoresinol dimethyl ether and lirioresinol-B dimethyl ether; the other two were new lignans, magnolin and fargesin, and their structures have been determined by spectroscopic studies.

INTRODUCTION

A CHINESE drug 'shin-i' was described in Shen Lung Pen Tsao Chen, A.D. 25, a classical Chinese herbal book, and has been used for the treatment of nasal empyema and headache. The flower buds of *Magnolia* spp. (Magnoliaceae) have been used as the source of the drug. From anatomical studies, K. Kimura *et al.*[1,2] reported that Chinese 'Shin-i' was made from flower buds of *M. fargesii* Cheng, and Japanese 'Shin-i' from *M. salicifolia* Maxim or M. *kobus* DC.

K. Kimura *et al.*[2] found α-pinene, cineol, chavicol methyl ether and citral in the essential oil of *Magnolia fargesii*. An alkaloid with empirical formula $C_{17}H_{19}O_3N$ was isolated by M. Kimura *et al.*[3] Hayashi and Ouchi[4] obtained rutin from the flowers of *M. kobus* DC. and recently Hirose *et al.*[5] found that the seed of this plant contains sitosterol, sesamin and lirioresinol-B dimethyl ether as unsaponifiable components. We have isolated four neutral lignans from dried flower buds of *M. fargesii*; the present report deals with the structures of these lignans.

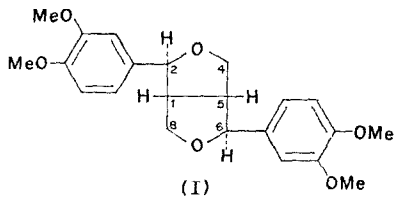
RESULTS

Compound B

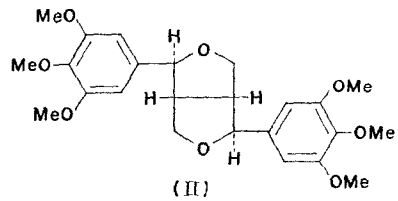
The molecular formula, $C_{22}H_{26}O_6$, was assigned from elemental analysis and the mass spectrum. The NMR spectrum showed the presence of 4 methoxyl groups and 8 aliphatic protons as well as 6 aromatic protons; it also showed only 13 protons in different environments rather than 26 (see $C_{22}H_{26}O_6$). These facts and the other spectral properties indicated that B had structure I, with absolute stereochemistry[6] as shown. I is known as pinoresinol

[1] K. KIMURA, K. HATA and M. YOSHIZAKI, *Japan J. Pharmacog.* **15**, 50 (1961).
[2] K. KIMURA, K. HATA and M. YOSHIZAKI, *Japan J. Pharmacog.* **16**, 18 (1962).
[3] M. KIMURA, M. YOSHIZAKI, I. MURO and D. SHIHO, *J. Pharm. Soc. Japan* **85**, 570 (1965).
[4] K. HAYASHI and K. OUCHI, *Rep. Instit. Nat. Res.* **14**, 1 (1949).
[5] M. HIROSE, Y. SATO and A. HAGITANI, *J. Chem. Soc. Japan* **89**, 887, 889 (1968).
[6] K. FREUDENBERG and G. S. SIDHU, *Chem. Ber.* **94**, 851 (1961); B. CARNMALM, *Arkiv. Kemi.* **15**, 215 (1960)

dimethyl ether, and the physical properties and IR spectrum of B were coincident with those reported for this lignan.[7] The mass spectrum is discussed later.



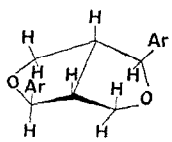
(I)
Pinoresinol dimethyl ether



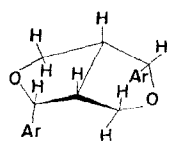
(II)
Lirioresinol-B dimethyl ether

Compound D

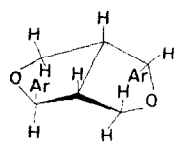
D is very similar to B, and its chemical and physical properties show it has structure II, with the absolute configuration as shown. II is known as lirioresinol-B dimethyl ether, and properties of D agree with those reported for this lignan.[8] The stereochemistry of lirioresinol-B dimethyl ether was determined from the NMR spectrum, which showed 6 methoxyl groups at δ 3·8 and 3·84 ppm and 8 aliphatic protons between 3·1 and 4·7 ppm as well as 4 aromatic protons at 6·53 (s) ppm. As with pinoresinol dimethyl ether, the NMR showed only 15 protons in different environments rather than 30. Thus, lirioresinol-B dimethyl ether must have a symmetrical stereochemistry as in III or IV and cannot have structure V, in which one



(III)



(IV)



(V)

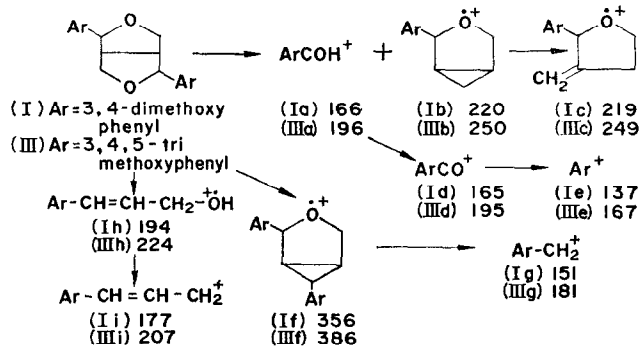
phenyl group is in the *exo*-position and the other in the *endo*-position. Differentiation between structures III and IV was made by detailed analysis of the NMR spectrum. Aliphatic protons attached to carbon atoms bearing the ether oxygen (C_2–H, C_4–H, C_6–H, and C_8–H) of lirioresinol-B dimethyl ether all appeared at a lower field than δ 4·1 ppm. Birch reported that the *endo*-aryl group in 3,7-dioxabicyclo[3,3,0]octane is held very close to the *endo*-hydrogen atom on the opposite ring, so this atom resonates upfield from the normal position by anisotropic effect of the aromatic ring.[9] These facts eliminate structure IV, because C_4–H and C_8–H in this compound would appear at higher fields than δ 4·0 ppm. The stereochemistry of lirioresinol-B dimethyl ether can therefore be assigned as III.

Compound C

The molecular formula of this new compound, magnolin, is $C_{23}H_{28}O_7$ from the elemental analysis and the mass spectrum. All the oxygen atoms are involved in ether linkages since the IR spectrum lacked both hydroxyl and carbonyl absorption. The NMR and MS showed that it is a lignan containing a 3,7-dioxabicyclo[3,3,0]octane skeleton. The gross

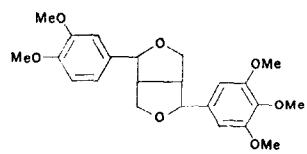
[7] W. M. HEARON and W. S. MCGREGON, *Chem. Rev.* **55,** 957 (1955).
[8] E. E. DICKEY, *J. Org. Chem.* **23,** 179 (1958); P. R. JEFERIES, and D. E. WHITE, *Austral. J. Chem.* **14,** 175 (1961).
[9] A. J. BIRCH, P. L. MACDONALD and A. PELTER, *J. Chem. Soc.* **C,** 1968 (1967).

structure of this new lignan was deduced by comparing its MS with those of (I) and (II). Mass spectra of I and II are very similar, except that the fragments of the pinoresinol dimethyl ether are 30 m.u. lower than those of lirioresinol-B dimethyl ether. The main fragmentation patterns[10] of the two compounds are shown in Scheme 1.

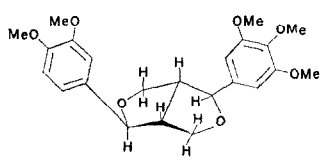


SCHEME 1.

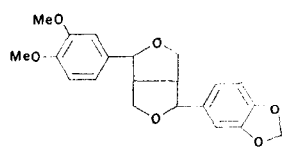
Mass spectral patterns of magnolin are more complicated than those of I and II, since the spectrum reveals two series of fragmentations. The peaks in one series have 30 m.u. higher mass number than those of the second series, and furthermore, the two fragmentation series are very similar to those of I and II, respectively. Thus magnolin has the 3,7-dioxabicyclo[3,3,0]octane skeleton, the C_2- and C_3-positions of which have trimethoxyphenyl



(VI)



Magnolin (VII)



(VIII)

and dimethoxyphenyl groups attached, respectively (see VI). This was confirmed from the observation that simple addition of the MS of I and II led to a composite almost identical with the spectrum of magnolin.

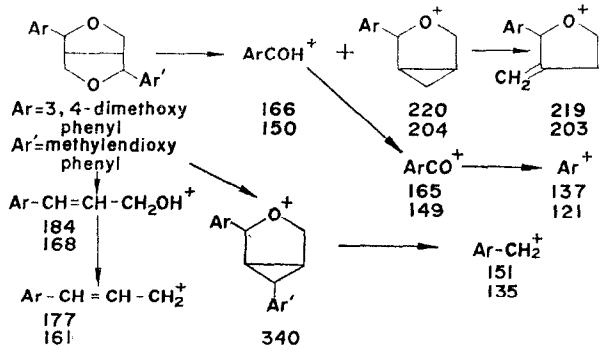
The NMR spectrum showed the presence of 5 methoxyl groups at δ 3·90 ppm. Aromatic protons appeared at two positions 6·55 and 6·90 ppm, and their shapes and chemical shifts are almost the same as those of I and II, respectively. The UV spectrum of magnolin was also closely related to the UV of I and II. Magnolin thus contains 3,4-dimethoxyphenyl and 3,4,5-trimethoxyphenyl groups. Aliphatic protons appeared at δ 3·15 (*m*, 2H), 4·2–4·45 (*m*, 2H), and 4·8 (*d*, J = 4 Hz, 2 Hz), and no signal was found between 3·2 and 3·9 ppm. These NMR features show that magnolin has the same stereochemistry as I and II, and can be represented by structure VII. The optical rotation of magnolin was exactly half way between those of I and II, so the absolute configuration of magnolin is as in VII.

Compound A

The molecular formula, $C_{21}H_{22}O_6$, of this new compound, fargesin, was assigned from the elemental analysis and the MS, and is the same as pinoresinol dimethyl ether except that there is one $-CH_2$ less. The structure of this new lignan was determined from the MS and NMR spectra.

[10] A. PELTER, *J. Chem. Soc.* C, 1376 (1967).

The MS of this lignan is as complicated as that of magnolin, and reveals the two series of fragmentation patterns. One series is almost the same as that in the spectrum of pinoresinol dimethyl ether, and the members of the other series have 16 m.u. smaller mass



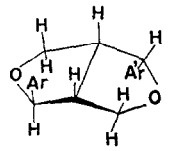
SCHEME 2.

number; the pattern is very similar to that of sesamin.[10] Thus fargesin was clearly a 2-dimethoxyphenyl-6-methylen-dioxyphenyl-3,7-dioxabicyclo[3,3,0]octane (VIII). The presence of dimethoxyphenyl and methylendioxyphenyl groups was confirmed from the NMR spectrum, which showed 2 methoxyl groups at 3·90 ppm, methylenedioxy group at 3·95 and 6 aromatic protons at 6·8–6·95 ppm. The NMR spectrum of fargesin was different from those of the other lignans. In the case of di-*exo*-diphenyl lignans (e.g. I), the spectra show only half the protons in different environments, because the molecule is symmetrical. In

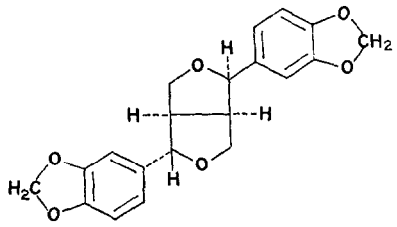
TABLE 1. THE NMR SPECTRA OF LIGNANS

Protons	Fargesin	Epieudesmin (X)	Pinoresinol dimethyl ether
1H	2·9 m	2·9 m	3·12 m
2H	4·88 d(J = 5)	4·85 d(5·5)	4·78 d(4)
4H	3·35 m	3·25–3·45 m	4·2–4·4 m
	3·6–4·0 m	3·7–3·9 m	3·8–4·0 m
5H	3·35 m	3·3 m	—
6H	4·45 d(7)	4·45 d(7)	—
8H	3·6–4·0 m	3·7–3·9 m	—
	4·1–4·25 m	4·1–4·4 m	—
OCH_3	3·90 s	—	3·86, 3·88
O_2CH_2	5·95 s		—
Aromatic	6·85–6·96 m		6·8–7·0

the case of fargesin, the benzylic hydrogen at C-2 showed a doublet at 4·88 (J = 5 Hz) distinct from that due to C_6-H at 4·45 (*d*, J = 7 Hz), and the methine hydrogen (2·9 ppm) at C-1 was clearly different from that at C-5 (3·35 ppm). Furthermore, one of C_4–methylene hydrogens is moved upfield (2·9 ppm) from the normal position (4·2–4·4 ppm). Thus, the *endo*-C_4-hydrogen is within the shielding cone of the aromatic ring, and which must be held in the *endo*-position on the opposite ring. These features are very similar to those of epieudesmin which has one phenyl in the *endo*-position and the other in the *exo*-position (X) (see Table 1). Thus the stereochemistry of fargesin is as in IX.



Fargesin (IX)
(Ar groups as in VIII)



Epieudesmin (X)

EXPERIMENTAL

Isolation of the lignans. The material used for the present study was purchased from a Chinese herbal shop in Taipei, and was identified as flower bud of *M. fargesii.* Pulverized material was extracted with 96% EtOH by refluxing for 3 hr. The hot mixture was filtered from the residue, which was re-extracted (×3). The combined filtrates were concentrated to dryness under reduced pressure. The brown residue was treated with a warm 2% tartaric acid solution and filtered. This procedure was repeated until all the basic substances were removed. The acid-insoluble residue was extracted with boiling 96% EtOH (×4), and the combined extracts were concentrated to a brown jelly. The brown jelly was first treated with *n*-hexane and the insoluble part was then dissolved in ether. The ether solution was concentrated to dryness and the product was chromatographed on E. Merck Kieselgel and eluted with $CHCl_3$–Me_2CO–EtOH (50:1:0·2). Four crystalline fractions were obtained. The first three fractions were repeatedly recrystallized from ether to yield A, B, and C, and the fourth fraction was recrystallized from ethanol to give D.

Compound B (*pinoresinol dimethyl ether*). M.p. 106°. $[\alpha]_D$ +68·6° ($CHCl_3$) *Anal.* Found: C, 68·35; H, 6·78%; MW 286 by MS. Calc. for $C_{22}H_{26}O_6$: C, 68·38; H, 6·78%; MW 386. IR(KBr): 1592, 1513, 1265, 1020, 810, 850 cm^{-1}. NMR (δ ppm from TMS): 3·15 (*n*, 2H), 3·88 and 3·86 (12 H). 4·2–4·4 (m, 2H), 4·75 (*d*, J = 4 Hz, 2H), 6·85 (m, 6H). M.p. of the dibromide: 172°.

Compound D (*lirioresinol-B dimethyl ether*). M.p. 119–121°. $[\alpha]_D$ +48° ($CHCl_3$). *Anal.* Found: C, 64·94; H, 6·82%; MW 446 by MS. Calc. for $C_{24}H_{30}O_8$: C, 64·56; H, 6·77%; MW 446. IR (KBr): 1590, 1512, 1250, 1050, 830 cm^{-1}. NMR (δ from TMS): 3·1 (*m*, 2H), 3·8–3·84 (*m*, 18 H), 4·1–4·5 (*m*, 4H), 4·7 (*d*, 2H, J = 4·5 Hz), 6·53 (4 H). M.p. of the dibromide: 154–155°.

Compound C (*magnolin*). M.p. 96–97°. $[\alpha]_D$ +55·7° ($CHCl_3$). *Anal.* Found: C, 66·48; H, 6·87%; MW 416 by MS. Calc. for $C_{23}H_{28}O_7$: C, 66·33; H, 6·78%, MW, 416. λ_{max} 231 (ε 12 600), 280 nm (2900). IR (KBr): 1590, 1520, 1508, 1265, 1245, 1020, 850, 837, 800 cm^{-1}. NMR (δ from TMS): 3·15 (*m*, 2H), 3·85 and 3·90 (15 H), 4·2–4·45 (*m*, 2H), 4·8 (*d*, J = 4 Hz, 2H), 6·55 (*s*, 2H), 6·90 (*m*, 3H).

Compound A (*fargesin*). M.p. 138–139°. *Anal.* Found: C, 68·07; H, 6·24%; MW, 370 by MS. Calc. for $C_{21}H_{22}O_6$: C, 68·09; H, 5·99%; MW, 370. λ_{max} 233 (ε 10 800), 284 nm (5800). IR (KBr): 1605, 1590, 1505, 1240, 1020, 920, 810, 860 $cm.^{-1}$

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