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ISOLATION AND STRUCTURE OF MAGNOSALIN AND MAGNOSHININ, NEW NEOLIGNANS FROM MAGNOLIA SALICIFORIA MAXIM

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The structures of magnosalin and magnoshinin, new neolignans isolated from buds of *Magnolia salicifolia* MAXIM., were determined to be 1 and 4, respectively, on the basis of chemical and spectroscopic evidence.

KEYWORDS —— magnosalin; magnoshinin; neolignan; Shin-i; *Magnolia salicifolia*

Dried buds of several *Magnolia* species are well known as a crude drug "Shin-i" and used in some Chinese medical prescriptions, especially for nasal empyema. Chemical investigation on their constituents has been done by several authors, but it mainly concerned so far with the essential oils.[1] A few lignans[2] and an unidentified alkaloid[3] were also reported.

In Japan, mostly the buds of *Magnolia salicifolia* MAXIM. (Japanese name: tamushiba) are used as "Shin-i".[4] In the course of our search for biologically active substances from this plant, we isolated four phenolic alkaloids[5] and two new neolignans, named magnosalin and magnoshinin. The present communication describes the isolation and structure elucidation of the latter compounds.

Air-dried plant material (1 Kg), collected at Toga-mura District, Toyama Prefecture, was roughly pulverized and extracted with ether at room temperature and then with boiling MeOH. Each extract was separated into basic, acidic, and neutral fractions in the usual manner. The neutral fraction of the MeOH extract, after removal of the essential oil by steam distillation, was subjected to alkaline hydrolysis and the neutral fraction of the hydrolyzate was roughly separated by silica gel column chromatography using hexane, hexane-CH_2Cl_2, CH_2Cl_2, and MeOH-CH_2Cl_2. The CH_2Cl_2 eluate was further separated by preparative TLC on Merck Kieselgel 60 PF_{254} with benzene to give magnosalin (1) (140 mg) and magnoshinin (4) (105 mg).

Magnosalin (1), mp 98-99°C (from ether-hexane), $[\alpha]_D$ 0° ($CHCl_3$),[6] has the molecular formula $C_{24}H_{32}O_6$ and showed IR absorptions at 1612, 1600, and 1515 cm^{-1} and UV bands at 208, 231, and 298 nm (log ε: 4.61, 4.23, and 4.03). Its mass spectrum showed characteristic peaks at m/z 208 (base peak, $C_{12}H_{16}O_3^+$) and 360 ($M^+ - CH_3CH{=}CHCH_3$) along with the molecular ion peak at m/z 416. The NMR spectrum exhibited signals at δ 1.17

(6H, diffused d,[7] J=6 Hz, sec-CH_3 x 2), 1.75 (2H, m, CH_3-C<u>H</u>-CH x 2), and 3.27 (2H, diffused d,[7] J=9 Hz, Ar-C<u>H</u>-CH x 2) as shown in Fig. 1, suggesting a symmetric feature of its structure. Decoupling and NOE experiments between the signals at δ 1.75 and δ 3.27 clearly indicated that the hydrogens concerned are in vicinal, *cis*-arrangement. Furthermore, NOE's were observed between methoxyls, aromatic hydrogens, and benzylic hydrogens (Fig. 1).

From the above observations, two possible structures, 1 (racemate) and 2, can be deduced. Here, we propose the structure 1 for magnosalin, because a serious steric strain may be expected in the alternative structure 2.

It should be noted that recently Yamamura et al.[8] isolated a novel neolignan, heterotropan, from *Heterotropa takaoi* MAEKAWA and established its structure to be 3. Magnosalin, a stereoisomar of 3, is the second example of this class of neolignan having a cyclobutane system.

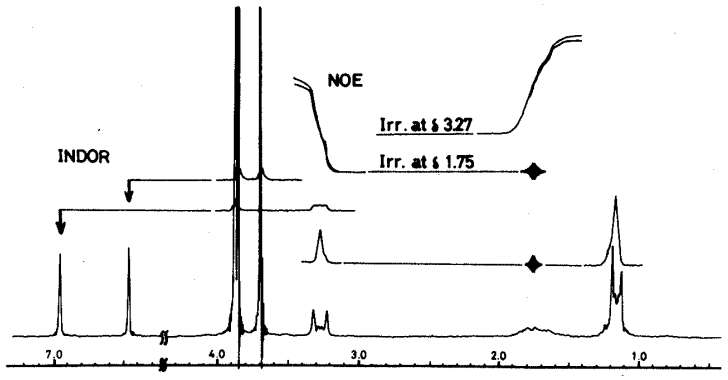
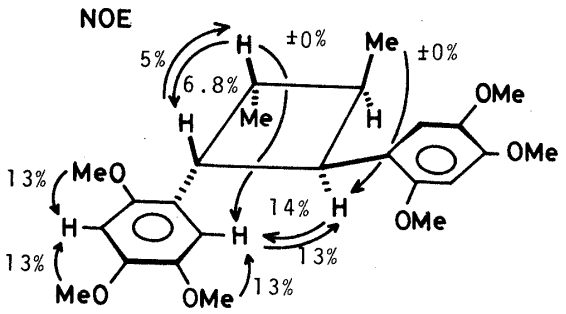
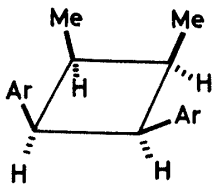


Fig.1. NMR (Normal, INDOR, and NOE) Spectra of Magnosalin ($CDCl_3$, 90 MHz)



1



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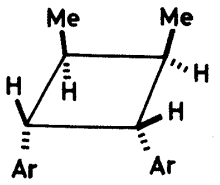
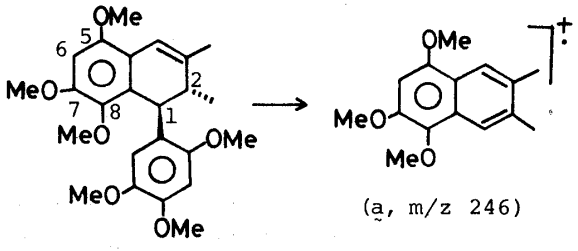


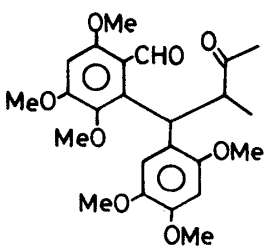
3

(Ar = 2,4,5-Trimethoxyphenyl)



4

(a, m/z 246)



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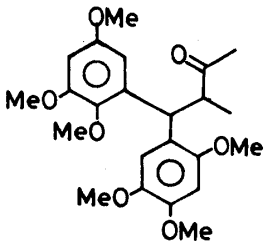

6

Magnoshinin (4), mp 113.5-115°C (from ether), $[\alpha]_D$ 0° ($CHCl_3$),[6] has the molecular formula $C_{24}H_{30}O_6$ and showed UV absorptions at 232, 260_{sh}, 269, 278, 292_{sh},

310, and 320 nm (log ε: 4.32, 4.11, 4.21, 4.22, 3.96, 3.95, and 3.92), suggesting the presence of a styrene chromophore. Its mass spectrum showed significant peaks at m/z 414 (base peak, M^+), 399, 383 (M^+-OCH_3), 368, 246 (a, M^+-$C_9H_{12}O_3$), and 231.[9] The NMR spectrum ($CDCl_3$) exhibited signals at δ 1.10 (3H, d, J=6 Hz, sec-CH_3), 1.76 (3H, d, J=1.5 Hz, CH=C-CH_3), 2.27 (1H, dq, J=0.8, 6 Hz, CH-CH-CH_3), 3.44, 3.61, 3.97 (each 3H, s, OCH_3 x 3), 3.90 (9H, s, OCH_3 x 3), 4.70 (1H, d, J=0.8 Hz, Ar-CH-CH), 6.33, 6.49, 6.59 (each 1H, s, aromatic H), and 6.57 (1H, q, J=1.5 Hz, Ar-CH=C-CH_3) and their splitting patterns were easily analyzed by the decoupling method.

The above data, coupled with the biogenetic consideration, led us to suppose that the structure of magnoshinin might be 4, in which the stereochemistry of 1,2-substituents may be *trans*-diaxial from the coupling constant (0.8 Hz) between 1- and 2-hydrogens.[10]

In order to confirm the substitution pattern of methoxyl groups on the dihydronaphthalene nucleus, we next examined the degradation of 4. Osmium tetroxide oxidation of 4, followed by HIO_4 oxidation, afforded a keto-aldehyde (5), $C_{24}H_{30}O_8$, mp 131-132°C, IR (KBr) ν_{max}: 1700 and 1670 cm^{-1}, NMR ($CDCl_3$): δ 2.08 (3H, s, $COCH_3$), 6.40, 6.44, 7.18 (each 1H, s, aromatic H), and 10.62 (1H, s, CHO).

Selective decarbonylation of 5 with tristriphenylphosphinerhodium chloride[11] in benzene gave a decarbonyl compound (6) in 12% yield, oil, $C_{23}H_{30}O_7$ (M^+: 418.2035. Calcd: 418.1992), NMR ($CDCl_3$): δ 1.01 (3H, d, J=7 Hz, sec-CH_3), 2.04 (3H, s, $COCH_3$), 3.39 (1H, dq, J=11.5, 7 Hz, CH-CH_3), 3.62, 3.76 (each 3H, s, OCH_3 x 2), 3.78, 3.85 (each 6H, s, OCH_3 x 4), 4.99 (1H, d, J=11.5 Hz, Ar-CH-CH), 6.34, 6.58 (each 1H, d, J=3 Hz, aromatic H), 6.50, and 6.78 (each 1H, s, aromatic H).

Thus the structure of magnoshinin was established to be 4 (racemate).[12]

Biological activities of 1 and 4 are currently under investigation.

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6) The CD curves of 1 and 4 showed no Cotton effect. We are grateful to Dr. H. Ishii and Dr. T. Ishikawa, Chiba University, for CD measurements.
7) Complex pattern may be due to virtual coupling.
8) S. Yamamura, M. Niwa, M. Nonoyama, and Y. Terada, *Tetrahedron Lett.*, 4891 (1978). We are grateful to Dr. S. Yamamura, Keio University, for the copies of NMR and IR spectra of heterotropan for comparison.
9) We are indebted to Dr. A. Kato, Niigata College of Pharmacy, for high-resolution MS measurement of magnoshinin.
10) F. D. Hostettler and M. K. Seikel, *Tetrahedron*, 25, 2325 (1969); A. F. A. Wallis, *Tetrahedron Lett.*, 5287 (1968); *idem, Aust. J. Chem.*, 26, 585 (1973) and references cited therein.
11) J. Tsuji and K. Ohno, *Tetrahedron Lett.*, 3969 (1965).
12) The 5,6,7-trisubstituted structure is excluded from the biogenetic point of view.

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