Magnone A and B, Novel Anti-PAF Tetrahydrofuran Lignans from the Flower Buds of Magnolia fargesii

ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · JULY 1998

Impact Factor: 3.8 · DOI: 10.1021/np970445+ · Source: PubMed

8 AUTHORS, INCLUDING:

Sei-Ryang Oh
Korea Research Institute of Bioscience and …
180 PUBLICATIONS **1,899** CITATIONS
SEE PROFILE

Si Hyung Park
Mokpo National University
55 PUBLICATIONS **614** CITATIONS
SEE PROFILE

Hwa-Young Lee
Soon Chun Hyang University Hospital
328 PUBLICATIONS **5,619** CITATIONS
SEE PROFILE

Pergamon

PII: S0031-9422(98)00040-5

Phytochemistry, Vol. 48, No. 8, pp. 1383–1386, 1998

Printed in Great Britain
0031-9422/98/$—see front matter

5α,7α(H)-6,8-CYCLOEUDESMA-1β,4β-DIOL FROM THE FLOWER BUDS OF *MAGNOLIA FARGESII*

KEUN YOUNG JUNG, DONG SEON KIM, SI-HYUNG PARK, IM SEON LEE, SEI RYANG OH, JUNG JOON LEE, EUN-HEE KIM†, CHAEJOON CHEONG† and HYEONG-KYU LEE*

Natural Product Biosynthesis Research Unit, Korea Research Institute of Bioscience and Biotechnology, Yusong P.O. Box 115, Taejon 305-600; † Magnetic Resonance Group, Korea Basic Science Institute, Taejon 305-333, Korea

(*Received in revised form* 22 *October* 1997)

Key Word Index—*Magnolia fargesii*; Magnoliaceae; cycloeudesmane-type sesquiterpene; 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol.

Abstract—From the Chinese crude drug *shin-i*, the flower buds of *Magnolia fargesii*, a new cycloeudesmane-type sesquiterpene, 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol, was isolated. The structure was elucidated by means of various NMR techniques. This compound has biogenetic significance because it is a plausible intermediate of the oppositol-type compound such as homalomenol A reported from this plant. © 1998 Elsevier Science Ltd. All rights reserved

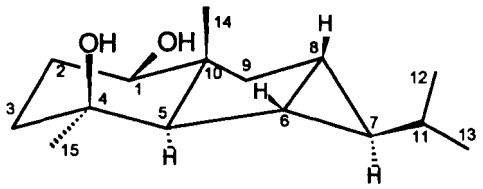
INTRODUCTION

The dried flower buds of *Magnolia fargesii* has a history of use for the treatment of nasal congestion with headache, sinusitis, and allergic rhinitis [1]. Pharmacological studies have revealed that *shin-i* has uterus-stimulating, hypotensive, antifungal, and skeletal muscle contracting effects [2, 3]. In previous reports on chemical investigations of this plant, many kinds of essential oils, lignans, neolignans and sesquiterpenes have been found and pharmacological activities of these lignans from *shin-i*, Ca^{2+} antagonistic activity and platelet activating factor (PAF) antagonistic activity were revealed [4–10].

Recently, we reported the structural elucidation of the four sesquiterpenes, oplopanone, oplodiol, homalomenol A and 1β,4β,7α-trihydroxyeudesmane isolated from the ethyl acetate extracts of this plant besides seven know phenolic lignans with PAF antagonistic activity [11]. In a continuing study, we have isolated a new cycloeudesmane-type sesquiterpene, 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol (**1**) from this plant.

RESULTS AND DISCUSSION

An ethyl acetate extract of the flower buds of *M. fargesii* was fractionated by repeated column chromatography (silica gel and RP-18) to yield compound **1** as colorless needles.



1

Compound **1** revealed an absorption at 3401 cm^{-1} in its IR spectrum suggesting the presence of a hydroxyl group. The EI mass spectrum of **1** exhibited a molecular ion peak at *m/z* 238 and the significant fragmentation ion peaks at *m/z* 220 $[M-H_2O]^+$, 202 $[M-2H_2O]^+$, 195 $[M-C_3H_7]^+$, 177 $[220-C_3H_7]^+$ and/or $[195-H_2O]^+$, indicating the presence of at least two hydroxyl groups and a propyl group.

The ^1H NMR spectrum of **1** in $CDCl_3$ showed a methine proton attached a hydroxyl function at δ 3.33 (1H, *dd*, *J* = 10.9 and 4.4 Hz), two tertiary methyl proton at δ 1.30 (3H, *s*) and 1.17 (angular Me, *s*), and an isopropyl group at δ 0.93 (3H, *d*, *J* = 6.6 Hz), 0.97 (3H, *d*, *J* = 6.6 Hz) and 0.98 (1H, *m*), which was further confirmed by ^1H–^1H COSY and HMBC spectra. The ^{13}C NMR and DEPT spectra suggested that the skeleton consisted of 15 carbons: four methyls, three methylenes, six methines and two quartenary carbons. From the HMQC spectrum of **1**, the chemi-

*Author to whom correspondence should be addressed. Tel. +82-42-860-4413; Fax. +82-42-860-4608; e-mail: hykylee@kribb4680.kribb.re.kr.

Table 1. ^1H and ^{13}C NMR Assignments for 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol (**1**)

Position	^1H		^{13}C	
	δ_H[a]	δ_H[b]	δ_C[a]	δ_C[b]
1	3.33 (1H, *dd*, 10.9, 4.4)	3.27 (1H, *dd*, 11.4, 4.3)	78.04 (*d*)	78.99
2	1.72 (1H, *m*)	1.76 (1H, *m*)	28.20 (*t*)	28.89
	1.61 (1H, *m*)	1.49 (1H, *m*)		
3	1.66 (1H, *m*)	1.64 (1H, *m*)	39.57 (*t*)	40.42
	1.35 (1H, *m*)	1.38 (1H, *m*)		
4			70.98 (*s*)	71.52
5	0.71 (1H, *d*, 4.6)	0.69 (1H, *d*, 5.7)	60.61 (*d*)	62.15
6	1.17 (1H, *m*)	1.32 (1H, *m*)	23.97 (*d*)	25.37
7	0.52 (1H, *m*)	0.45 (1H, *ddd*, 8.8, 3.0. 3.0)	49.89 (*d*)	51.12
8	1.18 (1H, *m*)	1.13 (1H, *m*)	24.37 (*d*)	25.50
9	0.91 (1H, *m*)	0.83 (1H, *m*)	44.48 (*t*)	45.81
	1.84 (1H, *m*)	1.82 (1H, *m*)		
10			58.03 (*s*)	59.40
11	0.98 (1H, *m*)	0.88 (1H, *m*)	32.48 (*d*)	33.94
12	0.93 (3H, *d*, 6.6)	0.96 (3H, *d*, 6.5)	21.87 (*q*)	22.29
13	0.97 (3H, *d*, 6.6)	0.98 (3H, *d*, 6.5)	21.73 (*q*)	22.29
14	1.17 (3H, *s*)	1.16 (3H, *d*, 0.9)	15.51 (*q*)	16.23
15	1.30 (3H, *s*)	1.28 (3H, *s*)	30.28 (*q*)	30.54

[a]Assignments were based on DEPT, ^1H-^1H COSY, HMQC and HMBC in $CDCl_3$.
[b]Measured in CD_3OD.

cal shifts of protonated carbons were assigned as listed in Table 1. Characteristic ^{13}C NMR signals of δ 78.04 (CH), 70.98 (C), 58.03 (C), 30.28 (CH_3) and 15.51 (CH_3) suggested a eudesmane skeleton with one secondary and one tertiary hydroxyl group. In addition, three methine carbon signals at δ 23.97, 24.37 and 49.89, which appeared in the significantly high field region, indicated the presence of a 1,2,3–trisubstituted cyclopropane ring [12]. In the HMBC correlations, two methyl proton signals of an isopropyl group were correlated to the carbon signals at 32.48 (C-11) and 49.89 (C-7), and the latter was correlated with the proton signals at δ 0.71 (H-5) and 1.84 (H-9). Also, in the cyclopropane ring moiety, the methine carbon signals at δ 23.97 (C-6) and 24.37 (C-8) were correlated with the proton signal of H-5 and H-9, respectively. The methyl proton signal at δ 1.17 (H-14) was long-range-correlated to the methine carbon signal at δ 60.61 (C-5) to which the proton signals at δ 3.33 (H-1) and 0.52 (H-7) were correlated. All the remaining proton signals were correlated to proximate carbon signals through two and/or three bond connections as shown Fig. 1. Thus, the structure of **1** could be assigned from the above evidence; its stereochemistry was determined as described below.

The configuration of the hydroxyl group at C-1 was confirmed to be in the equatorial position (β) from the fact that the coupling constants (*dd*, J = 10.9 and 4.4 Hz) of H-1 in the ^1H NMR spectrum indicated its axial position [13]. Regarding the configuration of the hydroxyl at C-4, an axial orientation (β) will result in deshielding of the methyl carbon (C-15) and a downfield shift in its resonance to approximately δ 30 [14, 15]. An equatorial orientation (α) results in the C-15 carbon having a chemical shift of approximately δ 25 [16, 17]. The corresponding signal observed in the ^{13}C NMR spectrum is δ 30.28 and this value agrees well with the assignment of the axial orientation. The stereochemistry of C-7 was deduced through the observation of the NOESY spectrum of **1** in CD_3OD solution because the signals of H-6, H-8 and the methyl proton of C-14 in the ^1H NMR spectrum in $CDCl_3$ were very much overlapped. The NOESY spectrum of **1** showed strong interactions between the proton at δ 0.69 (H-5) and the proton at δ 0.45 (H-7), and no interaction of the proton at δ 1.16 (H-14) with H-7 and H-11. This result indicated that the configurations of the isopropyl moiety and the proton of C-7 are equatorial and axial orientations, respectively, as shown in the proposed structure (chair con-

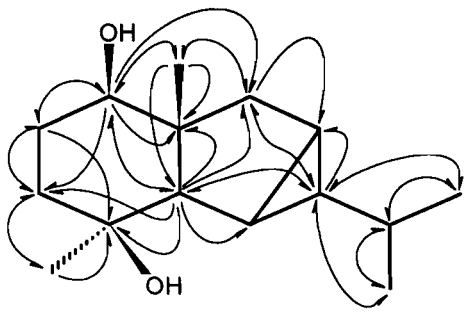
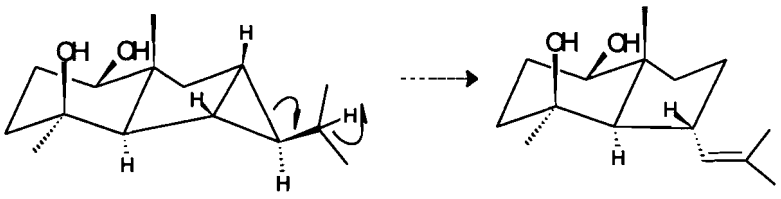


Fig. 1. HMBC correlations for 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol (**1**). The arrow indicate correlations from proton to carbon.



1 2

Scheme 1. The possible biogenetic conversion of **1** into homalomenol A (**2**).

formation). All of these findings established that the structure of **1** was 5α,7α(H)-6,8-cycloeudesma-1β,4β-diol (**1**), a new cycloeudesmane-type sesquiterpene.

The reports of cycloeudesmane-type sesquiterpenes show that they are very rare in nature [18]. In the case of the 6,8-cycloeudesmane-type, Itokawa *et al.* [12] have reported the isolation of 1β-hydroxy-6,8-cyclo-4(15)eudesmene from the plant *Torilis japonica*. This compound was also obtained by the biomimetic reaction of epoxygermacrene-D with basic alumina [19]. Therefore, compound **1** has a biogenetic significance because it is a plausible intermediate of the oppositol-type of compound such as homalomenol A (**2**) [11] isolated from this plant (Scheme 1).

EXPERIMENTAL

Mps: Electrothermal 9100, uncorr. Optical rotation was recorded on Jasco DIP-370 digital polarimeter. The IR and UV spectra were recorded using a Magna 550 spectrophotometer in KBr pellet and a Milton Roy Spectronic 3000 Array spectrophotometer in MeOH soln, respectively. The EI-MS spectra were performed on a Hewlett-Packard 5889A. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker DRX-300 spectrometer and the chemical shifts were referenced to TMS as the internal standard. HMBC and NOESY data were recorded on a Bruker DMX-600 spectrometer. CC was carried out on Kieselgel 60 (Merck No. 9385 and 7729) and LiChroprep RP-18.

Plant material

The dried flower buds of *Magnolia fargesii* Cheng was purchased from Il-Shin Pharm. Co. (Taejon, Korea) which imported the material from China. A voucher specimen is deposited in our laboratory (NDC-052).

Extraction and isolation

The dried and pulverized flower buds of *M. fargesii* (3 kg) were extracted with MeOH at room temp. for several days. The MeOH extracts were concentrated under red. press. to give a residue (225 g). The residue was partitioned between *n*-hexane (40 g), EtOAc (109 g), *n*-BuOH (20 g) and H_2O, in the usual order. The EtOAc extract was loaded on silica gel CC eluted with a stepwise solvent gradient of MeOH in $CHCl_3$ to afford nineteen subfractions. The subfr. 8 (3 g) was further purified by repeated RP-18 (MeOH–H_2O, 3:2) and SiO_2 CC ($CHCl_3$–MeOH, 99:1) to give compound **1** (24 mg).

5α,7α(H)-6,8-cycloeudesma-1β,4β-diol (*1*). Colorless needles in MeOH; mp 146–147°. $[\alpha]_D^{25}$ −4.0° (*c* 0.25, $CHCl_3$). IR $[\nu]_{max}^{KBr}$ cm^{-1}: 3401, 2949, 1015. EI-MS *m/z* (rel. int.): 238 $[M]^+$ (6), 220 (51), 205 (21), 202 (18), 195 (14), 187 (40), 177 (54), 159 (100). ^{1}H NMR (300 MHz): Table 1. ^{13}C NMR (75 MHz): Table 1.

REFERENCES

1. Namba, T., *Coloured Illustrations of Wakan-Yaku* (*The Crude Drugs in Japan, China and Neighbouring Countries*), Vol. II. Hoikusha Publishing, Osaka, 1980, pp. 127–129.
2. Tang, W. and Eisenbrand, G., *Chinese Drugs of Plant Origin: Chemistry, Pharmacology, and Use in Traditional and Modern Medicine*. Springer-Verlag, Berlin, 1992, pp. 639–646.
3. Chen, C. C., Huang, Y. L., Chen, H. T., Chen, Y. P. and Hsu, H. Y., *Planta Medica*, 1988, **54**, 438.
4. Miyazawa, M., Kasahara, H. and Kameoka, H., *Phytochemistry*, 1992, **31**, 3666.
5. Miyazawa, M., Ishikawa, Y., Kasahara, H., Yamanaka, J. I. and Kameoka, H., *Phytochemistry*, 1994, **35**, 611.
6. Miyazawa, M., Kasahara, H. and Kameoka, H., *Phytochemistry*, 1996, **42**, 531.
7. Chen, C. C., Huang, Y. L., Chen, H. T., Chen, Y. P., Hsu, H. Y. and Kuo, Y. H., *Chemical and Pharmaceutical Bulletin*, 1988, **36**, 1791.
8. Kakisawa, H., Kusumi, T., Hso, H. Y. and Chen, Y. P., *Bulletin of Chemical Society of Japan*, 1970, **43**, 3631.
9. Hwang, Y. L., Chen, C. C., Chen, Y. P., Hsu, H. Y. and Kuo, Y. H., *Planta Medica*, 1990, **56**, 237.
10. Pan, J. X., Hensens, O. D., Zink, D. L., Chang, M. N. and Hwang, S. B., *Phytochemistry*, 1987, **26**, 1377.
11. Jung, K. Y., Kim, D. S., Oh, S. R., Lee, I. S., Lee, J. J., Lee, H. K., Shin, D. H., Kim, E. H. and

Cheong, C.-J., *Archives Pharmacal Research*, 1997, **20**, 363.
12. Itokawa, H., Matsumoto, H. and Mihashi, S., *Chemistry Letters*, 1983, 1253.
13. Nyasse, B., Tih, R. G., Sondengam, B. L., Martin, M. T. and Bodo, B., *Phytochemistry*, 1988, **27**, 179.
14. Herz, W. and Watanabe, K., *Phytochemistry*, 1983, **22**, 1457.
15. Sung, T. V., Steffan, B., Steglich, W., Klebe, G. and Adam, G., *Phytochemistry*, 1992, **31**, 3515.
16. Toyota, M. and Asakawa, Y., *Phytochemistry*, 1990, **29**, 3664.
17. Zhao, Y., Yue, J.-M., He, Y.-N., Lin, Z.-W. and Sun, H.-D., *Journal of Natural Products*, 1997, **60**, 545.
18. Connolly, J. D. and Hill, R. A., *Directory of Terpenoids, Vol.* 1. *Mono- and Sesquiterpenoids*, Chapman & Hall, London, 1991, pp. 394–397.
19. Yamamura, S., Niwa, M., Ito, M. and Saito, Y., *Chemistry Letters*, 1982, 1681.