

Lignans from the Flower Buds of *Magnolia fargesii*

Jun Lee, Min Suk Yang, Sang Hae Nam,[†] Mi Yae Shon,[†] Seon Woo Hwang, and Ki Hun Park*

Division of Applied Life Science (BK21 program), Department of Agricultural Chemistry, Gyeongsang National University, Jinju 660-701, Korea. *E-mail: khpark@gsnu.ac.kr

[†]Department of Food Science, Jinju National University, Jinju 660-758, Korea

Received February 16, 2005

The three new lignans **1-3** were isolated from the methanol extracts of the flower buds of *Magnolia fargesii*. They were elucidated as (7*S*,8*R*)-1-(3,4-dimethoxyphenyl)-2-*O*-(2-methoxy-4-omegahydroxypropylphenyl) propane-1,3-diol, (7*S*,8*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-*O*-(6-hydroxy-2-methoxy-4-omegahydroxypropylphenyl) propane-1,3-diol, and [tetrahydro-4-hydroxy-2-(3,4,5-trimethoxyphenyl)furan-3-yl]methyl 3,4-dimethoxy benzoate by spectral analysis.

Key Words : *Magnolia fargesii*, Magnoliaceae, Lignan, Phenylpropanoid, Phenylfuranoid

Introduction

Magnolia fargesii (Magnoliaceae) continues to be a rich source of new secondary metabolites with wide biological activity such as anti-platelet-activating factor (PAF), anti-TNF α , and calcium antagonism.¹⁻⁵ In particular, specific parts of the flower buds of this species have been used as an important source of Chinese drugs as well as biologically active lignans.^{6,7} Lignans are classified as polyphenolic compounds, which present in various natural foods are known to show some health-enhancing effects.⁸ Previous chemical investigation carried out on this species shows that most lignans have a C6-C6-C6 (furofuran or furan) system.^{4,6,7,9,10} Here, we report on the isolation and structural elucidation of the new phenylpropanoids, (7*S*,8*R*)-1-(3,4-dimethoxyphenyl)-2-*O*-(2-methoxy-4-omegahydroxypropylphenyl) propane-1,3-diol (**1**) and (7*S*,8*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-*O*-(6-hydroxy-2-methoxy-4-omegahydroxypropylphenyl) propane-1,3-diol (**2**). Also we wish to report the structurally rare phenylfuranoid (C6-C5-*O*-C7 system), [tetrahydro-4-hydroxy-2-(3,4,5-trimethoxyphenyl)-furan-3-yl]methyl 3,4-dimethoxy benzoate (**3**) (Fig. 1).

Results and Discussion

Compounds **1** and **2** were obtained as sticky oils in only small amounts from the flower buds of *Magnolia fargesii*. Compound **1** was found to have the molecular formula of

C₂₁H₂₈O₇ with eight degrees of unsaturation from HREIMS (m/z 392.1830). HMQC spectrum and DEPT experiments in the ¹³C-NMR showed carbon signals for 3 methyl, 4 methylene, 8 methine and 6 quaternary carbons. Hence the eight degrees of unsaturation were presumed to be due to two aromatic rings. The propanyl group was easily defined with the connectivity from C-7 to C-9 in ¹H-¹H COSY spectrum. The phenylpropanoid unit was certified by HMBC correlation between H-7 resonating at δ 4.96 with C-2 (δ 109.2) and C-6 (δ 118.3). Two unassigned methoxy groups in phenylpropanoid unit were easily determined because each methoxy group was correlated with C-3 and C-4 in the HMBC. Omegahydroxypropylphenyl group was proved by the connectivity from H-7' to H-9' and allylic coupling between H-2' and H-7' in ¹H-¹H COSY spectrum. The methoxy group in C-3' was determined by a correlation between CH₃O, C-3', and H-2' in the HMBC. This propanoid group was attached to the C-8 position because the H-8 proton resonating at δ 4.11 displayed HMBC connectivity with C-4'. Additionally, a mass fragment at m/z 167 (M⁺-225) indicated that a substituent of C-8 could be a 1'-hydroxypropyl-3'-methoxyphenyl group. The 8*R*-configuration of **1** was confirmed with negative signs at 210-250 nm in CD spectra.¹¹⁻¹⁴ The *erythro* configuration of **1** was predicted by NMR coupling constant ($J_{7,8} = 4.4$ Hz).¹¹⁻¹⁴ Thus, compound **1** is deduced to have (7*S*,8*R*)-configuration. Consequently, the structure of compound **1** was determined to be (7*S*,8*R*)-1-(3,4-dimethoxyphenyl)-2-*O*-(2-methoxy-4-

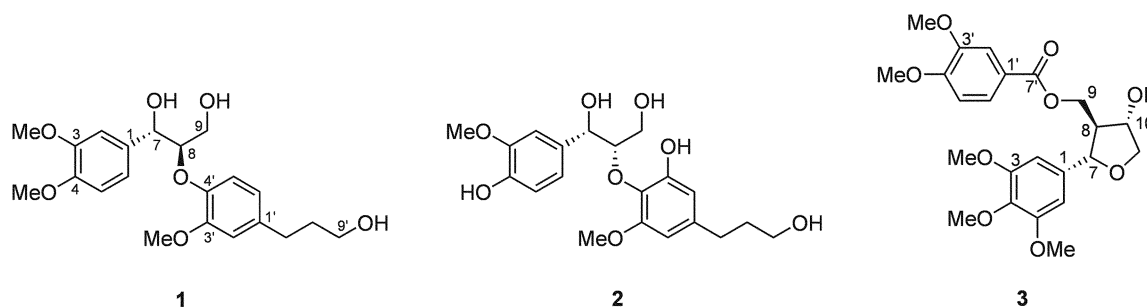


Figure 1. Structures of lignans 1-3.

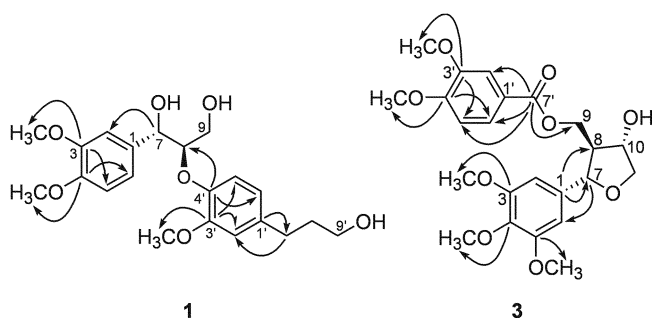


Figure 2. Selected correlations in HMBC spectra of compounds **1** and **3**.

omegahydroxypropylphenyl) propane-1,3-diol.

Compound **2** has the molecular formula of $C_{20}H_{26}O_8$ with eight degrees of unsaturation as deduced from the HREIMS (m/z 394.1592), suggesting two aromatic rings. The 1H - 1H COSY spectrum of **2** revealed good connectivity to infer the same skeleton with **1**. Based on the 1H -NMR, ^{13}C -NMR spectra and MS fragment at m/z 181 ($M^+ - 225$) of **2**, methoxy group at C-4 changed into hydroxy group and one more hydroxy group appeared at C-5' comparing with compound **1**. In HMBC experiment, the C-4 showed a correlation with H-2, H-5, and H-6, whereas the C-3 has a correlation with H-2 and H-5 supported a 3-methoxy-4-hydroxyphenyl moiety. 1',3',4',5'-Tetrasubstituted phenyl ring was deduced from the singlet of H-2' (δ 6.67) and H-6' (δ 6.67), whose carbon signals were appeared at δ 113.0 and δ 116.4, respectively. The (7*S*,8*S*)-absolute configuration of **2** was also confirmed with the positive signs (215-245 nm) in CD spectra and larger coupling constant ($J_{7,8} = 7.3$ Hz).¹¹⁻¹⁴ Therefore, compound **2** was proved as (7*S*,8*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-*O*-(6-hydroxy-2-methoxy-4-omegahydroxypropylphenyl) propane-1,3-diol.

The IR spectrum of **3** showed absorptions at 3459 and 1709 cm^{-1} , suggesting the presence of hydroxy and ester groups. Its mass data indicated to have the molecular formula of $C_{23}H_{28}O_9$ with ten degrees of unsaturation, as deduced from its HREIMS (m/z 448.1741). HMQC spectrum and DEPT experiments in the ^{13}C -NMR showed two aromatic rings and a carbonyl group. Hence, extra degrees of unsaturation were presumed to be due to a tetrahydrofuran ring. The successive connectivities of from H-7 to H-11, and between H-2 and H-7 in 1H - 1H COSY spectrum supported a phenylfuran skeleton. Symmetric methoxyl signal (δ 3.84, 6H, s), symmetrical aromatic signal (δ 6.66, 2H, s) and another methoxyl signal supported 3,4,5-trimethoxyphenyl group, which was linked to C-7 in tetrahydrofuran ring, since a correlation between H-7 and C-2 was observed in HMBC. Dimethoxybenzoyl moiety was proved by presence of MS fragment at m/z 165 ($M^+ - 283$), ABX-system signals at δ 6.88 (1H, d, $J = 8.4$ Hz), 7.50 (1H, d, $J = 2.0$ Hz), 7.58 (1H, dd, $J = 2.0, 8.4$ Hz), and two methoxyl singlets (δ 3.91, 3.94). The 3',4'-dimethoxybenzoyl moiety was shown to be condensed with 9-OH of phenylfuranoid, since a correlation was observed between H-9 (δ 4.47) and the carbonyl carbon (δ 166.6) of dimeth-

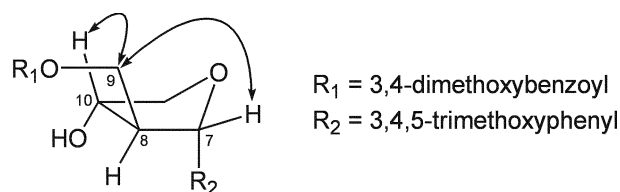


Figure 3. Selected correlations in NOESY spectrum of compound **3**.

oxybenzoyl moiety. NOE relationships in 2D-NOESY and the coupling constant of H-7 ($J = 8.0$ Hz) suggested all trans orientations for H-7/H-8 and H-8/H-10 respectively. NOE cross peaks were observed between H7-H9 and H9-H10, whereas NOEs were not observed between H7-H8 and H8-H10 (Fig. 3). Compound **3** ($[\alpha]_D^{20} +34.0$, $CDCl_3$) was identified as [tetrahydro-4-hydroxy-2-(3,4,5-trimethoxyphenyl)furan-3-yl]methyl 3,4-dimethoxy benzoate, whose skeleton was only reported by Iida, T *et al.*¹⁵

Experimental Section

Instruments. Optical rotations were obtained using a Perkin-Elmer polarimeter. IR spectra were recorded on a Bruker IFS66 infrared Fourier transform spectrophotometer (KBr) and UV spectra were measured on a Beckman DU650 spectrophotometer. CD spectra were obtained with a JASCO 715 spectropolarimeter. NMR experiments were conducted either on a Bruker (AM 500 MHz) FT-NMR or a Varian Inova (400, 500 MHz) with tetramethylsilane (TMS) as internal standard. EIMS and HREIMS were recorded on a Jeol JMS-700 instrument operated at 70 eV. TLC analysis were performed on Kieselgel 60 F₂₅₄ (Merck) plates and silica gel (230-400 mesh) was used for column chromatography.

Extraction and isolation. The flower buds of *Magnolia fargesii* were purchased from Daechang Oriental Herb Store in Jinju, South Korea. A voucher specimen (Lee, J. & M. S. Yang 021) was deposited at the Herbarium of Gyeongsang National University (GNCU). The air-dried flower buds (1 kg) of *Magnolia fargesii* were extracted with MeOH (5 L \times 3) at room temperature. The combined extracts were concentrated *in vacuo* to afford a brown gum (67 g), which was partitioned with chloroform and water. The chloroform layer was washed with brine, dried over anhydrous Na_2SO_4 , and then concentrated to give a thickish residue (34 g). The residue was chromatographed on Silica gel (650 g) column eluting with a gradient of 100% of chloroform to 100% MeOH to afford 76 fractions (F1-F76, each 120 mL). F37-42^(A) were further chromatographed on silica gel with gradient mixture of chloroform and acetone (49 : 1 \rightarrow 1 : 1, each 50 mL) to give 45 subfractions A1-A45. Fractions A22-A23 were further purified with silica gel chromatography eluting with chloroform and acetonitrile (9 : 1 \rightarrow 1 : 1) to afford compound **3** (6 mg, $R_f = 0.48$, $CHCl_3$ -acetone = 2 : 1). The fractions F47-F51^(B) were carried out silica gel chromatography with gradient mixture of chloroform and acetone (19 : 1 \rightarrow 1 : 1, each 50 mL) to give 42 subfractions B1-B42. Fractions B24-B25 were further purified by

Table 1. ^{13}C -NMR data for compounds 1-3

Position	1	2	3
1	132.5 (s)	133.6 (s)	136.7 (s)
2	109.2 (d)	109.3 (d)	103.5 (d)
3	148.8 (s)	147.1 (s)	153.7 (s)
4	148.2 (s)	146.0 (s)	137.9 (s)
5	110.9 (d)	114.7 (d)	153.7 (s)
6	118.3 (d)	119.8 (d)	103.5 (d)
7	72.6 (d)	88.3 (d)	83.8 (d)
8	87.0 (d)	54.2 (d)	56.2 (d)
9	60.7 (t)	64.4 (t)	63.6 (t)
10			75.4 (d)
11			75.0 (t)
1'	137.8 (s)	135.8 (s)	122.2 (s)
2'	112.3 (d)	113.0 (d)	112.2 (d)
3'	151.0 (s)	144.6 (s)	149.0 (s)
4'	144.7 (s)	128.2 (s)	153.6 (s)
5'	120.3 (d)	147.0 (s)	110.5 (d)
6'	121.1 (d)	116.4 (s)	123.8 (d)
7'	31.8 (t)	32.4 (t)	166.6 (s)
8'	34.2 (t)	35.0 (t)	
9'	62.0 (t)	62.7 (t)	
OMe			
3	55.88 (q)	56.40 (q)	56.33 (q)
4	55.85 (q)		61.0 (q)
5			56.33 (q)
3'	55.88 (q)	56.45 (q)	56.25 (q)
4'			56.30 (q)

chromatography on silica gel eluting with chloroform and acetonitrile (4 : 1 \rightarrow 1 : 1) to afford compound **1** (11 mg, R_f = 0.45, CHCl_3 -acetonitrile = 2 : 3) and **2** (7.0 mg, R_f = 0.51, CHCl_3 -acetonitrile = 2 : 3).

(7S,8R)-1-(3,4-Dimethoxyphenyl)-2-O-(2-methoxy-4-omegahydroxypropylphenyl)propane-1,3-diol (1): Sticky oils; UV λ_{max} (CHCl_3) nm (log ϵ): 279 (3.79); IR ν_{max} (KBr) cm^{-1} : 3452, 1743, 1728, 1691, 1628, 1565, 1550; CD ($c = 2.66 \times 10^{-3}$ M, MeOH) $\Delta\epsilon$ (nm): -0.59 (220), -0.98 (239); $^1\text{H-NMR}$ δ_{H} (CDCl_3 , 400 MHz): 1.85 (2H, m, H-8'), 2.64 (2H, t, $J = 7.6$ Hz, H-7'), 3.64 (3H, t, $J = 6.4$ Hz, H-9'/H-9a), 3.84 (3H, s, 4-OMe), 3.85 (6H, s, 3, 3'-OMe), 3.89 (1H, m, H-9b), 4.11 (1H, dd, $J = 5.6, 8.4$ Hz, H-8), 4.96 (1H, d, $J = 4.4$ Hz, H-7), 6.71 (1H, dd, $J = 1.6, 8.0$ Hz, H-6'), 6.74 (1H, d, $J = 1.6$ Hz, H-2'), 6.83 (2H, d, $J = 8.0$ Hz, H-5/H-5'), 6.89 (1H, dd, $J = 1.6, 8.0$ Hz, H-6), 6.96 (1H, d, $J = 1.6$ Hz, H-2); $^{13}\text{C-NMR}$ δ_{C} (CDCl_3 , 100 MHz): See Table 1; EIMS m/z (70 eV, rel. int.): 392 [M^+] (2.9), 374 (1.4), 344 (3.4), 270 (1.9), 242 (6.3), 210 (5.6), 208 (100); HREIMS m/z [M^+]: Calcd. for $\text{C}_{21}\text{H}_{28}\text{O}_7$: 392.1835. Found: 392.1830.

(7S,8S)-1-(4-Hydroxy-3-methoxyphenyl)-2-O-(6-hydroxy-2-methoxy-4-omegahydroxypropylphenyl)propane-1,3-diol (2): Sticky oils; UV λ_{max} (CHCl_3) nm (log ϵ): 282 (3.84); IR ν_{max} (KBr) cm^{-1} : 3457, 1727, 1645, 1550, 1511; CD ($c = 2.17 \times 10^{-3}$ M, MeOH) $\Delta\epsilon$ (nm): +0.42 (227), +0.49 (233), +0.46 (237); $^1\text{H-NMR}$ δ_{H} (CDCl_3 , 500 MHz): 1.88

(2H, m, H-8'), 2.67 (2H, t, $J = 7.5$ Hz, H-7'), 3.60 (1H, dd, $J = 5.9, 12.0$ Hz, H-8), 3.69 (2H, t, $J = 6.3$ Hz, H-9'), 3.86 (3H, s, 3-OMe), 3.88 (3H, s, 3'-OMe), 3.94 (2H, m, H-9), 5.54 (1H, d, $J = 7.3$ Hz, H-7), 6.67 (2H, s, H-2'/H-6'), 6.88 (1H, d, $J = 8.1$ Hz, H-5), 6.91 (1H, dd, $J = 1.2, 8.3$ Hz, H-6), 6.94 (1H, s, H-2); $^{13}\text{C-NMR}$ δ_{C} (CDCl_3 , 125 MHz): See table 1; EIMS m/z (70 eV, rel. int.): 394 [M^+] (40.7), 376 (100), 364 (20.1), 331 (12.7), 317 (16.8), 299 (41.7), 283 (8.8), 251 (11.7), 181 (6.6). HREIMS m/z [M^+]: Calcd. for $\text{C}_{20}\text{H}_{26}\text{O}_8$: 394.1628. Found: 394.1592.

[Tetrahydro-4-hydroxy-2-(3,4,5-trimethoxyphenyl)furan-3-yl]methyl 3,4-dimethoxy benzoate (3): Sticky oils; $[\alpha]_{\text{D}}^{20} + 34$ (c 0.5, CHCl_3). UV λ_{max} (CHCl_3) nm (log ϵ): 265 (4.06), 290 (3.79); IR ν_{max} (KBr) cm^{-1} : 3459, 1709, 1644, 1594, 1511, 1460; $^1\text{H-NMR}$ δ_{H} (CDCl_3 , 400 MHz): 2.57 (1H, m, H-8), 3.83 (3H, s, 4-OMe), 3.84 (6H, s, 3, 5-OMe), 3.91 (3H, s, 3'-OMe), 3.94 (3H, s, 4'-OMe), 4.08 (2H, d, $J = 4.4$ Hz, H-11), 4.47 (3H, m, H-9/H-10), 4.63 (1H, d, $J = 8.0$ Hz, H-7), 6.66 (2H, s, H-2/H-6), 6.88 (1H, d, $J = 8.4$ Hz, H-5'), 7.50 (1H, d, $J = 2.0$ Hz, H-2'), 7.58 (1H, dd, $J = 2.0, 8.4$ Hz, H-6'); $^{13}\text{C-NMR}$ δ_{C} (CDCl_3 , 100 MHz): See Table 1; EIMS m/z (70 eV, rel. int.): 448 [M^+] (4.8), 316 (2.5), 300 (14.5), 285 (9.4), 265 (52.8), 256 (29.4), 182 (24.2), 165 (100); HREIMS m/z [M^+]: Calcd. for $\text{C}_{23}\text{H}_{28}\text{O}_9$, 448.1733. Found: 448.1741.

Acknowledgments. Research for this article was supported in part by a grant from the Brain Korea 21 program.

References

- Pan, J. X.; Hensens, O. D.; Zink, D. L.; Chang, M. N.; Hwang, S. B. *Phytochemistry* **1987**, *26*, 1377-1379.
- Chen, C. C.; Huang, Y. L.; Chen, H. T.; Chen, Y. P.; Hsu, H. Y. *Planta Med.* **1988**, *54*, 438-440.
- Chae, S. H.; Kim, P. S.; Cho, J. Y.; Park, J. S.; Lee, J. H.; Yoo, E. S.; Baik, K. U.; Lee, J. S.; Park, M. H. *Arch. Pharm. Res.* **1988**, *21*, 67-69.
- Jung, K. Y.; Kim, D. S.; Oh, S. R.; Park, S. H.; Lee, I. S.; Lee, J. J.; Shin, D. H.; Lee, H. K. *J. Nat. Prod.* **1998**, *61*, 808-811.
- Cho, J. Y.; Yoo, E. S.; Baik, K. U.; Park, M. H. *Arch. Pharm. Res.* **1999**, *22*, 348-353.
- Kakisawa, H.; Chen, Y. P.; Hsü, H. Y. *Phytochemistry* **1972**, *11*, 2289-2293.
- Miyazawa, M.; Kasahara, H.; Kameoka, H. *Phytochemistry* **1992**, *31*, 3666-3668.
- Cheong, W. J.; Park, M. H.; Kang, G. W.; Ko, J. H.; Seo, Y. J. *Bull. Korean Chem. Soc.* **2005**, *26*, 747-754.
- Kakisawa, H.; Kusumi, T.; Hso, H. Y.; Chen, Y. P. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3631.
- Miyazawa, M.; Kasahara, H.; Kameoka, H. *Phytochemistry* **1996**, *42*, 531-533.
- Francesca, C.; Brigida, D. B.; Marina, D.; Antonio, F.; Armando, Z. *J. Agric. Food Chem.* **2003**, *51*, 6165-6172.
- Stephane, B.; Danielle, R.; Jeanpierre, U.; Francois, R. T.; Karim, M. *J. Agric. Food Chem.* **2003**, *51*, 34-42.
- Marina, D. G.; Antonio, M.; Pietro, M.; Lucio, P. *Phytochemistry* **1994**, *35*, 777-779.
- Fang, J. M.; Lee, C. K.; Cheng, Y. S. *Phytochemistry* **1992**, *31*, 3659-3661.
- Iida, T.; Noro, Y.; Ito, K. *Phytochemistry* **1983**, *22*, 211-213.