



AN INSECT GROWTH INHIBITORY LIGNAN FROM FLOWER BUDS OF *MAGNOLIA FARGESII*

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Key Word Index—*Magnolia fargesii*; Magnoliaceae; shin-i; flower buds; lignan; (+)-epimagnolin A; insect growth inhibitor.

Abstract—Bioassay-guided isolation afforded a new lignan, (+)-epimagnolin A, from the flower buds of *Magnolia fargesii*. This lignan exhibited growth inhibitory activity against larvae of *Drosophila melanogaster*. The structure of a new lignan was determined on the basis of spectral methods.

INTRODUCTION

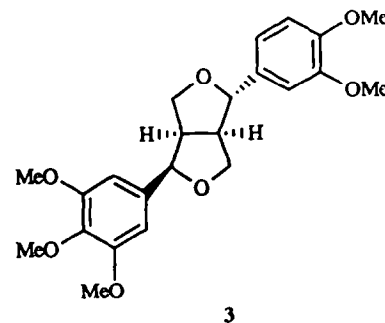
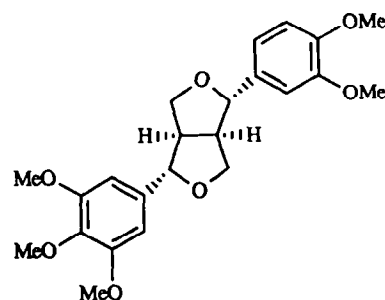
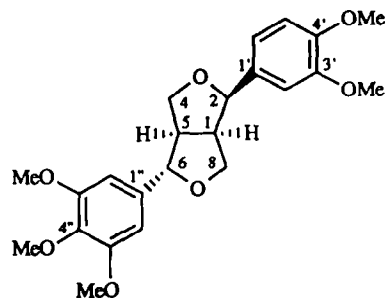
The Chinese crude drug shin-i, the flower buds of *Magnolia fargesii*, has a history of safe use and contains lignans and neolignans, which show biological activities [1, 2]. In the course of our studies on biologically active compounds from Chinese crude drugs, we found that shin-i had larval growth inhibitory activity against *Drosophila melanogaster*. Bioassay-guided isolation gave a new 2,6-diaryl-3,7-dioxabicyclo[3,3,0]octane type lignan, (+)-epimagnolin A.

Biological activity of this type of lignan against insects has been reported and revealed that kobusin and sesamin inhibited the growth of silkworms (*Bombyx mori*) [3]. Asarinin and sesamin also showed synergistic activity towards a wide variety of insecticides [4, 5]. Therefore, the investigations on insect larval growth inhibitory lignans are important. The present paper deals with the isolation, structural elucidation and insect larval growth inhibitory activity of the new lignan.

RESULTS AND DISCUSSION

Flower buds of *M. fargesii* were extracted with methanol for 10 hr under reflux, and a crude extract was obtained. This was reextracted successively with hexane, CH_2Cl_2 , butanol and water. Extraction with CH_2Cl_2 gave a crude reddish brown liquid with insecticidal activity. The CH_2Cl_2 soluble portion was fractionated by silica gel column chromatography and bioassayed using published methods [6, 7]. Subsequently, 1 was isolated as an active principle.

Compound 1 had a molecular formula $\text{C}_{23}\text{H}_{28}\text{O}_7$ as determined by mass spectrometry ($[\text{M}]^+ m/z$ 416) and NMR data. The molecular formula was consistent with that of magnolin (2) [8, 9] or epimagnolin (3) [10]. The ^1H NMR spectrum of 1 (Table 1) was similar to that of



phillygenin [8]. Therefore, the structure of **1** was deduced to be **3** from these results. However, the ^{13}C NMR spectral data of **1** were not coincident with those of **3** (Table 2). The carbon signals assigned to the veratryl group were consistent with those of phillygenin [8] (axial-veratryl type) and the signals of the 3,4,5-trimethoxyphenyl group were consistent with those of **2** (equatorial-3,4,5-trimethoxyphenyl type). These results allowed us to conclude that **1** was an antipode of epimagnolin (**3**) and it was named (+)-epimagnolin A.

The growth inhibitory effects of (+)-epimagnolin A against *D. melanogaster* were compared with controls and are reported in Table 3. The lignan showed significant growth inhibitory activity at concentrations greater than 1 mg ml^{-1} diet.

EXPERIMENTAL

Bioassay-guided isolation. Dried and pulverized flower buds of *M. fargesii* (1.86 kg) were extracted with MeOH for 10 hr under reflux. Solvent was removed under red. pres. to give an extract (370 g). The MeOH extract was extracted with hexane, CH_2Cl_2 , BuOH and H_2O . The CH_2Cl_2 sol. portion was subjected to silica gel CC and fractionated with hexane containing increasing concns of EtOAc. Isolation and bioassay were successively worked out and **1** (680 mg) was obtained. The bioassay for growth inhibitory activity against larvae of *D. melanogaster* Meigen was as follows; ca 100 adults from insect colonies were transplanted into a new culture bottle, in which a strip of wet folded filter paper was placed, and allowed to oviposit. After 3 hr, adults were removed from the culture

Table 1. ^1H NMR spectral data of (+)-epimagnolin A (**1**) and (+)-magnolin (**2**)

H	1	2
1	3.35 m	3.11 m
2	4.87 d (5.5)	4.77 d (5)
4 _{ax}	4.16 d (9.5)	3.92 dd (4, 9)
4 _{eq}	3.87 m	4.28 dd (7, 9)
5	2.92 m	3.11 m
6	4.44 d (7.2)	4.75 d (5)
8 _{ax}	3.35 m	3.92 dd (4, 9)
8 _{eq}	3.87 m	4.29 dd (7, 9)
2'	6.94 s	6.91 d (2)
5'	6.84 d (8)	6.84 d (8)
6'	6.88 d (8)	6.89 dd (2, 8)
2''	6.60 s	6.58 s
6''	6.60 s	6.58 s
OMe		
3'-	3.88 s	3.88 s
4'-	3.91 s	3.91 s
3''-	3.87 s	3.88 s
4''-	3.84 s	3.84 s
5''-	3.87 s	3.88 s

Recorded in CDCl_3 at 270 MHz. Chemical shifts in ppm downfield from TMS. Coupling constants in Hz.

Table 2. ^{13}C NMR spectral data of (+)-epimagnolin A (**1**) and (+)-magnolin (**2**)

C	1	2
1	49.9	54.1
2	81.8	85.7
4	70.8	71.7
5	54.4	54.4
6	87.6	86.0
8	69.6	71.9
1'	130.7	133.5
2'	108.8	109.2
3'	148.7	148.7
4'	147.8	149.0
5'	110.9	111.1
6'	117.5	118.2
1''	136.7	136.8
2''	102.7	102.8
3''	153.2	153.4
4''	137.3	137.5
5''	153.2	153.5
6''	102.7	102.8
OMe	55.7	55.9
	55.7	55.9
	55.9	56.2
	55.9	56.2
	60.5	60.9

Recorded in CDCl_3 at 270 MHz. Chemical shifts in ppm downfield from TMS. Coupling constants in Hz.

Table 3. Growth inhibitory effect of **1** in the *D. melanogaster* test

Sample	Dose in diet mg ml^{-1}	Numbers of pupae*			
		1†	2†	3†	Average
Compound 1	2	0	0	0	0.0
	1	0	3	0	1.0
	0.5	6	7	6	6.3
Control	—	10	10	9	9.7

*Five days after seeding 10 newly laid eggs on diet.

†Three replicates.

bottle and 10 newly laid eggs were collected and transplanted on to a diet containing the test material ($0.5\text{--}2\text{ mg ml}^{-1}$ diet) in a glass tube. Tubes were left for 5 days on 16 hr light/8 hr dark at 25° and 93% RH. The developmental stage and number of pupae were recorded, and compared with those of an untreated control.

(+)-Epimagnolin A. Yellowish oil. $[\alpha]_D +105.22^\circ$ (CHCl_3 ; c 3.45). IR ν_{max} cm^{-1} : 2939, 2840, 1592, 1517, 1029, 825. EIMS (probe, 70 eV) m/z (rel. int.): 416 ($[\text{M}]^+$, 100), 207 (10), 195 (33), 181 (22), 177 (27), 165 (23), 151 (29). NMR: Tables 1 and 2.

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