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Lignans from the Root of *Acanthopanax chiisanensis* Nakai

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ABSTRACT : Five lignans were isolated from the chloroform fraction of *Acanthopanax chiisanensis* Nakai root by open column chromatography. Their structures were elucidated as (-)-sesamin (1), helioxanthin (2), savinin (3), taiwanin C (4), and 3-(3",4"-dimethoxybenzyl)-2-(3',4'-methylenedioxybenzyl)butyrolactone (5) by spectral analysis. Among them, compounds 2, 3, 4, and 5 were isolated for the first time from this plant.

Key words : *Acanthopanax chiisanensis*, Araliaceae, 3-(3",4"-dimethoxybenzyl)-2-(3',4'-methylenedioxybenzyl) butyrolactone, helioxanthin, savinin, (-)-sesamin, taiwanin C

INTRODUCTION

Acanthopanax species belonging to Araliaceae are widely distributed in far East-Asian countries. The root and stem barks of *Acanthopanax* species have traditionally been used as a tonic, sedative as well as in the treatment of rheumatoid arthritis and diabetes mellitus (Hoe, 1951; Perry, 1980). Approximately fifteen species of *Acanthopanax* are grown in the Korean peninsula. Of them, *A. chiisanensis* is one of the most abundant indigenous species distributed at Mt. Jiri. Only a few studies on bioactive principles on this plant have been carried out. Constituents such as acanthoside D (Kim & Hahn, 1981), chiisanoside and its derivatives (Hahn *et al.*, 1984; Kasai *et al.*, 1986) and sesamin (Jang, 1970) have previously been evaluated from this plant. But there is no report on lactone-type lignans from this plant.

In this paper, we report the structure elucidation of constituents such as (-)-sesamin and lactone-type lignans for the first time from the root of *A. chiisanensis*.

MATERIALS AND METHODS

Plant Material

The root of *Acanthopanax chiisanensis* Nakai was collected at Kongju, Korea, and was authenticated by Seon Haeng Cho, Kongju National University of Education, Korea. The voucher specimen was deposited at the Herbarium of Natural Products Research Institute, Seoul National University, Korea.

Instruments and Reagents

IR spectra were recorded with a Jasco FT/IR-300E instrument on KBr disc. ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker AVANCE 400 NMR spectrometer in $CDCl_3$ using TMS as an internal standard. MS spectra were measured with a Jeol JMS-AX505WA mass spectrometer. Commercial grade reagents were used without further purification.

Extraction and Isolation

The air-dried powdered root (1.5 kg) of *A. chiisanensis* was extracted three times with methanol (3 × 3000

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mℓ) under reflux. The extract (159 g) thus obtained was partitioned between equal volumes of *n*-hexane (42 g) and water, and the aqueous layer was again partitioned successively with chloroform (26 g), ethyl acetate (10 g) and *n*-butanol (24 g).

A portion of the chloroform fraction (26 g) was chromatographed on silica gel column (7 × 60 ㎝) with a gradient elution of *n*-hexane and ethyl acetate to afford compounds 1 (26 ㎎, 95:5), 2 (45 ㎎, 90:10), 3 (33 ㎎, 87:23), 4 (27 ㎎, 80:20), and 5 (45 ㎎, 78:22).

Compound 1: $C_{20}H_{18}O_6$; $[\alpha]_D$: −87.2 (*c* 1.08, $CHCl_3$); IR ν_{max} (KBr): 1502, 1483, 1441, 1242, 1035 cm^{-1}; EI-MS (70 eV, rel. int., %): *m/z* 354 $[M]^+$ (100), 323 (12.6), 219 (7.5), 203 (34.7), 161 (64.8), 149 (90.6), 135 (53.8), 103 (8.3); ^{1}H-NMR (400 MHz, $CDCl_3$-*d*): δ6.87 (2H, d, *J* = 1.2 Hz, H-2',2"), 6.82 (2H, dd, *J* = 8.0, 1.2 Hz, H-6',6"), 6.79 (2H, d, *J* = 8.0 Hz, H-5',5"), 5.96 (2 × $-OCH_2O-$), 4.74 (2H, d, *J* = 4.2 Hz, H-2,6), 4.25 (2H, dd, *J* = 9.0, 6.8 Hz, H-4e,8e), 3.89 (2H, dd, *J* = 9.0, 3.5 Hz, H-4a,8a), 3.07 (2H, m, H-1,5); ^{13}C-NMR (100 MHz, $CDCl_3$-*d*): δ 147.9 (C-3',3"), 147.1 (C-4',4"), 135.0 (C-1',1"), 119.3 (C-6',6"), 108.1 (C-5',5"), 106.5 (C-2',2"), 101.0 (2 × $-OCH_2O-$), 85.7 (C-2,6), 71.7 (C-4,8), 54.3 (C-1,5).

Compound 2: $C_{20}H_{12}O_6$; IR ν_{max} (KBr): 1759, 1633, 1488, 1439, 1031 cm^{-1}; EI-MS (70 eV, rel. int., %): *m/z* 348 $[M]^+$ (100), 319 (16.2), 291 (7.7), 261 (5.1), 233 (6.4), 205 (4.2), 174 (6.1), 145 (4.5); ^{1}H-NMR (400 MHz, $CDCl_3$-*d*) and ^{13}C-NMR (100 MHz, $CDCl_3$-*d*): see Table 1.

Compound 3: $C_{20}H_{16}O_6$; IR ν_{max} (KBr): 1745, 1644, 1603, 1504, 1489, 1469, 1037, 926 cm^{-1}; EI-MS (70 eV, rel. int., %): *m/z* 352 $[M]^+$ (62.4), 217 (61.2), 189 (6.4), 159 (18.6), 135 (100), 131 (16.3), 103 (10.9), 77 (23.1); ^{1}H-NMR (400 MHz, $CDCl_3$-*d*) and ^{13}C-NMR (100 MHz, $CDCl_3$-*d*): see Table 2.

Table 1. ^{1}H- and ^{13}C-NMR data of compounds 2 and 4.

Carbons	2		4	
	^{1}H	^{13}C	^{1}H	^{13}C
1	-	139.7	-	140.1
2	-	121.5	-	134.6
3	-	121.0	-	134.6
4	8.45 (s)	127.4	7.71 (s)	118.9
5	7.73 (d 8.7)	125.4	7.22 (s)	103.6
6	7.33 (d 8.7)	111.8	-	148.6
7	-	146.9	-	149.9
8	-	147.4	7.14 (s)	103.6
9	-	130.4	-	130.5
10	-	129.0	-	128.3
1'	-	141.7	-	139.8
2'	6.83 (d 1.5)	109.6	6.83 (d 1.0)	110.5
3'	-	130.7	-	147.5
4'	-	130.7	-	147.5
5'	6.91 (d 7.7)	107.9	6.98 (d 7.8)	108.2
6'	6.81 (dd 7.7, 1.5)	122.3	6.81 (dd 7.8, 1.0)	123.4
$-OCH_2O-$	6.08 (dd 9.2, 1.2)	101.5	6.10 (s)	101.7
$-OCH_2O-$	5.98 (dd 9.2, 1.2)	101.2	6.08 (dd 8.0, 1.2)	101.2
C=O	-	171.1	-	169.7
Lactone CH_2	5.23 (q 15.2)	69.5	5.39 (d 0.6)	67.9

Table 2. ^{1}H- and ^{13}C-NMR data of compounds 3 and 5.

Carbons	3		5	
	^{1}H	^{13}C	^{1}H	^{13}C
1	-	172.5	-	178.5
2	-	125.8	2.57 (m)	46.4
3	3.76 (m)	39.9	2.49 (m)	41.2
4	4.27 (m)	69.5	4.15 (dd 9.1, 6.9)	71.2
			3.88 (dd 7.3, 1.9)	
α	7.51 (d 1.6)	137.2	2.96 (dd 14.1, 5.1)	34.7
			2.85 (dd 14.1, 7.0)	
β	3.00 (dd 14.2, 4.5)	37.5	2.60 (brd 7.3)	38.2
	2.61 (dd 14.2, 10.0)		2.52 (brd 7.9)	
1′	-	126.0	-	131.3
2′	7.06 (d 1.4)	109.1	6.60 (d 1.5)	109.4
3′	-	149.1	-	147.8
4′	-	148.3	-	146.4
5′	6.89 (d 8.1)	108.6	6.71 (d 7.7)	108.1
6′	7.09 (dd 8.1, 1.4)	128.1	6.58 (dd 7.7, 1.5)	122.2
1″	-	131.4	-	130.4
2″	6.68 (d 1.3)	108.8	6.49 (d 1.9)	111.7
3″	-	147.9	-	149.0
4″	-	146.5	-	147.8
5″	6.75 (d 7.9)	108.4	6.77 (d 8.1)	111.3
6″	6.65 (d 7.9, 1.3)	122.0	6.57 (dd 8.1, 1.9)	120.6
$-OCH_2O-$	6.06 (s)	101.7	5.93 (dd 4.2, 1.3)	101.1
$-OCH_2O-$	5.95 (brd 2.0)	101.0	-	-
OMe	-	-	3.86 (s)	55.9
OMe	-	-	3.83 (s)	55.7

Compound 4: $C_{20}H_{12}O_6$; IR ν_{max} (KBr): 1764, 1614, 1487, 1469, 1033 cm^{-1}; EI-MS (70 eV, rel. int., %): *m/z* 348 $[M]^+$(100), 319 (9.4). 289 (12.4), 261 (18.5), 233 (8.2), 159 (7.9); ^{1}H-NMR (400 MHz, $CDCl_3$-*d*) and ^{13}C-NMR (100 MHz, $CDCl_3$-*d*): see Table 1.

Compound 5: $C_{21}H_{22}O_6$; IR ν_{max} (KBr): 1768, 1590, 1487, 1515, 1504, 1487, 1034, 931 cm^{-1}; EI-MS (70 eV, rel. int., %): *m/z* 370 $[M]^+$ (92.7), 356 (22.1), 177 (34.9), 151 (94.6), 135 (100), 105 (13.1), 77 (20.9); ^{1}H-NMR (400 MHz, $CDCl_3$-*d*) and ^{13}C-NMR (100 MHz, $CDCl_3$-*d*): see Table 2.

RESULTS AND DISCUSSION

A chromatographic separation of the chloroform fraction from *A. chiisanensis* led to the isolation of compounds 1, 2, 3, 4, and 5.

Compound 1 was obtained as needles from MeOH. The IR spectrum of 1 showed absorption bands for CO (1035 cm^{-1}). The ^{1}H-NMR spectrum of 1 showed ABX splitting proton signals at δ6.87 (d, J = 1.2 Hz), 6.82 (dd, J = 8.0, 1.2 Hz) and 6.79 (d, J = 8.0 Hz). Furthermore, the singlet at δ5.96 showed the methylenedioxy signal in its structure. The ^{13}C-NMR

spectrum of 1 showed methylenedioxy signal at δ 101.0. The EI-MS of 1 showed an $[M]^+$ ion at *m/z* 354 as a base peak. The molecular formula of 1 was determined to be $C_{20}H_{18}O_6$ by the EI-MS. Accordingly the structure of 1 was elucidated as (-)-sesamin by comparing its spectral data in the literatures (Pelter *et al.*, 1978; Ina *et al.*, 1987).

Compound 2 was obtained as needles from MeOH. The IR spectrum of 2 showed characteristic signals of an α,β-unsaturated C=O (1759 cm^{-1}), olefinic double bond (1633 cm^{-1}), aromatic C=C (1488 cm^{-1}) and methylenedioxy group (1031 cm^{-1}). The ^{1}H-NMR spectrum of 2 revealed the presence of two methylenedioxy groups at δ6.08 and 5.98, one highly deshielded aromatic proton at δ8.45, and five more aromatic protons and an olefinic proton at δ6.81~7.73. The deshielding of one of the six aromatic protons indicated they were adjacent to the carbonyl group. Characteristic fragments of 2 were observed at *m/z* 348 $[M]^+$, 319, 291, 261, 233, 205, 174, and 145 in the mass spectrum. The molecular formula of 2 was determined to be $C_{20}H_{18}O_6$ by the EI-MS. In the ^{13}C-NMR spectrum of 2, 20 carbons were detected. Accordingly the structure of 2 was elucidated as helioxanthin by comparing its spectral data in the literature (Stevenson & Weber, 1989). Compound 4 was obtained as needles from MeOH. The features of spectra of 4 were similar to those of 2. But in the ^{1}H-NMR spectrum, H-5 and -8 signals of (A) ring were appeared as singlets at δ7.22 and 7.14, respectively. The EI-MS of 4 showed an $[M]^+$ ion at m/z 348 as a base peak. Accordingly the structure of 4 was elucidated as taiwanin C by comparing its spectral data in the literature (Stevenson & Weber, 1989).

Compound 3 was obtained as needles from MeOH. The IR spectrum of 3 showed characteristic to α,β-unsaturated C=O (1745 cm^{-1}), olefinic double bond (1644 cm^{-1}), aromatic nucleus (1489 cm^{-1}) and methylenedioxy group (926 cm^{-1}). The ^{1}H-NMR spectrum of 3 revealed the presence of two methylenedioxy groups at δ6.06 and 5.95. H-3 and -4 appeared as a multiplet at δ 3.76 and 4.27, respectively. The ^{1}H-NMR spectrum of 3 showed ABX splitting proton signals of (A) and (C) ring at δ7.09 (dd, J = 8.1, 1.4 Hz), 7.06 (d, J = 1.4 Hz), 6.89 (d, J = 8.1 Hz) and 6.75 (d, J = 7.9 Hz), 6.68 (d, J = 1.3 Hz), 6.65 (dd, J = 7.9, 1.3 Hz), respectively. Characteristic fragments of 3 were observed at *m/z* 352 $[M]^+$, 217, 189, 135 (base peak), 131, 103, 77 and 28 in the mass spectrum. The peaks at *m/z* 217 and 135 resulted from benzylic cleavage at the C-3 and β-position. The molecular formula of 3 was determined to be $C_{20}H_{18}O_6$ by the EI-MS. In the ^{13}C-NMR spectrum of 3, 20 carbons were detected. Accordingly the structure of 3 was elucidated as savinin by comparing its spectral data in the literatures (Banerji *et al.*, 1984; Shieh *et al.*, 1990). Compound 5 was obtained as needles from MeOH. The features of spectra of 5 were similar to those of 3. In the ^{13}C-NMR spectrum of 5, two methoxy

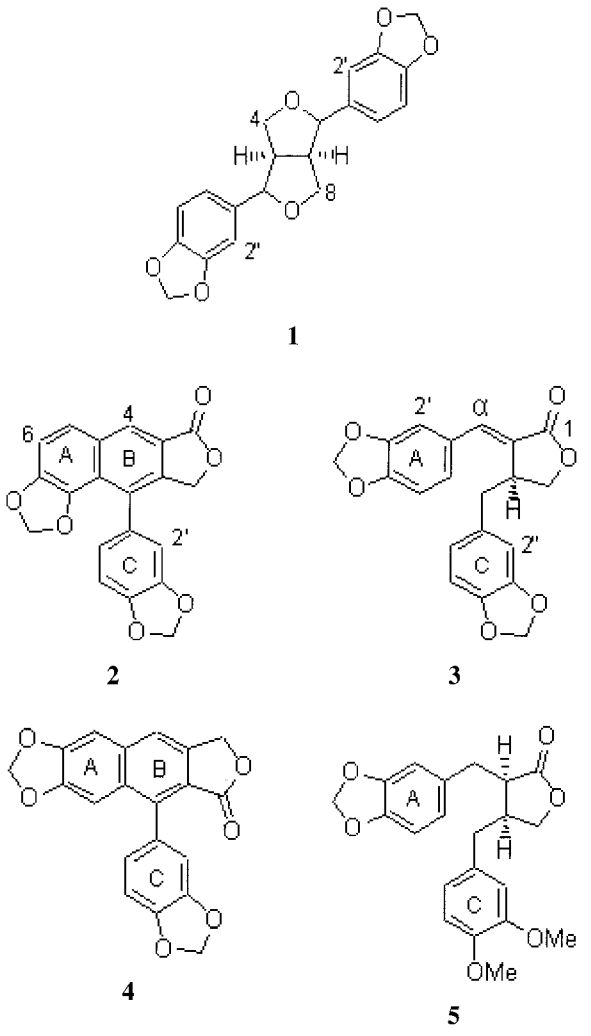

Fig. 1. Structures of compounds 1~5.

signals of (C) ring were observed at δ55.9 and 55.7. The EI-MS of 5 showed an $[M]^+$ ion at *m/z* 370. According to Corrie *et al.* (1970), relative configurations in 2,3-dibenzylbutyrolactone are given by NMR comparison of the methylene protons at C-4. Equivalence of these protons shape in the ^{1}H-NMR spectrum corresponds to the *cis*-configuration, while non-equivalence corresponds to the *trans*-configuration. In this respect, 5 must be *cis*-oriented by comparing equivalence of the methylene protons at C-4. Accordingly the structure of 5 was elucidated as 3-(3",4"-dimethoxybenzyl)-2-(3',4'-methylenedioxybenzyl)butyrolactone by comparing its spectral data in the literature (Lopes *et al.*, 1983).

Fig. 1 showed the structures of isolated lignans. But there is no report on lactone-type lignans from *A. chiisanensis*. Our report is the first to describe that helioxanthin (2), savinin (3), taiwanin C (4) and 3-(3",4"-dimethoxybenzyl)-2-(3',4'-methylenedioxybenzyl)butyrolactone (5) are the constituents of the roots of *A. chiisanensis*.

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