

A NEW LIGNAN, FORMOSALACTONE, FROM THE BARK OF
JUNIPERUS FORMOSANA HAY. VAR. CONCOLOR HAY.

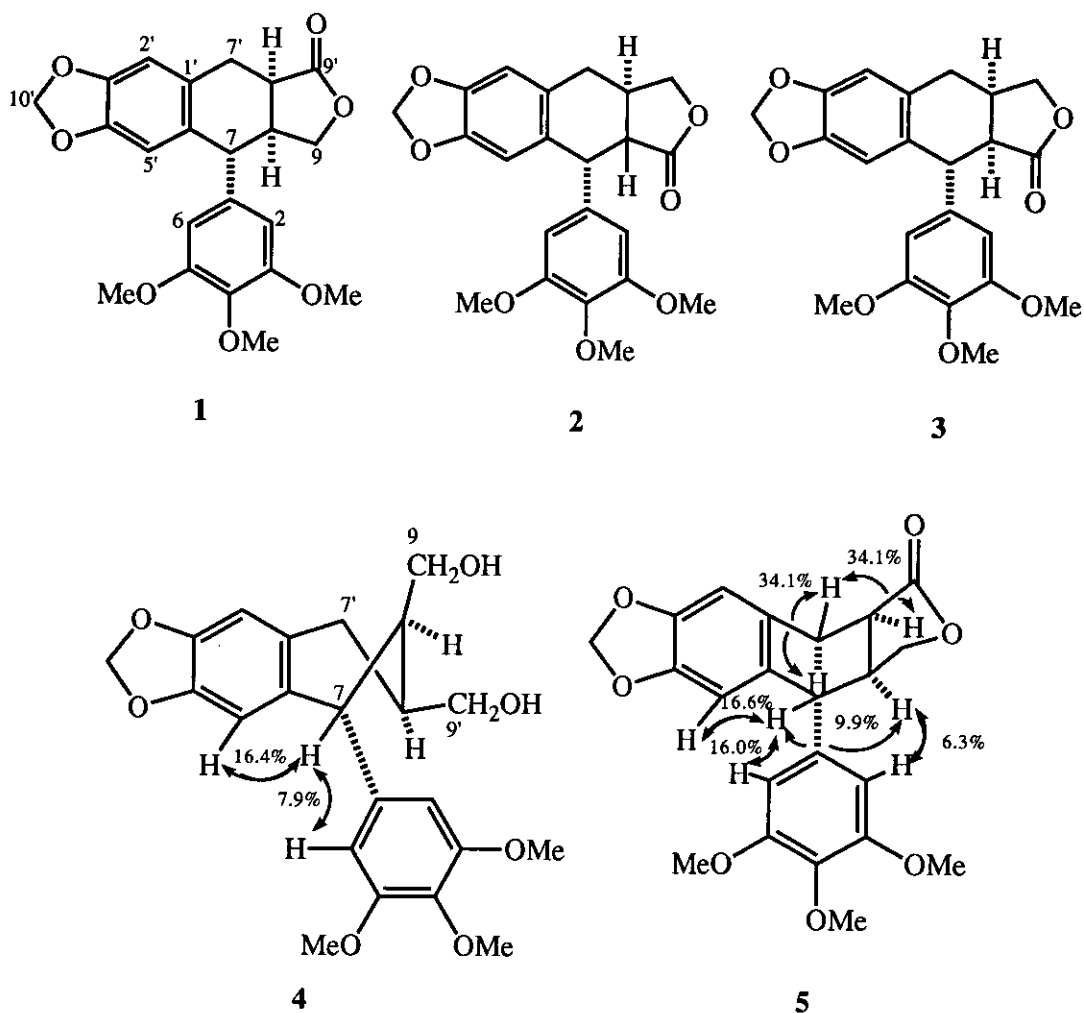
Yueh-Hsiung Kuo* and Ming-Tsang Yu

Department of Chemistry, National Taiwan University, Taipei, Taiwan, ROC

Abstract ----- The bark of *Juniperus formosana* Hay. var. concolor Hay. was found to contain a new lignan, formosalactone together with a known lignan, savinin. The structure has been elucidated by spectral evidence and chemical transformation.

Juniperus squamata Lamb var. *morrisonicola* (Hay.) Li and Keng, *J. formosana* Hay., and *J. formosana* Hay. var. *concolor* Hay. grow at an altitude of 2000-3000 m above sea level and *J. chinensis* Linn. and *J. chinensis* Linn. var. *kaizuca* Hort. are common ornamental tree.¹ In connection with our interest in lignans and terpenes, chemical investigation on the heartwoods of *J. squamata* Lamb var. *morrisonicola* (Hay.) Li and Keng (twelve known compounds in addition of five new sesquiterpenoids)² and *J. formosana* Hayata [fifteen known components together with six new compounds (including one sesquiterpene, two lignans, and tree diterpenes)]³ was undertaken in our laboratory. We focused our attention on the chemical studies of *J. formosana* Hay. var. *concolor* Hay. This paper deals with the structural elucidation of formosalactone (**1**). The air-dried barks of *J. formosana* concolor were repeatedly extracted with methanol. The methanol extracts were evaporated *in vacuo* to give a black residue which was purified on silical gel by repeated chromatography. One known lignan savinin⁴ and new lignan, formosalactone (**1**), were obtained, and the structural elucidation of formosalactone (**1**) is described as follows.

Formosalactone (**1**) was isolated as light yellow liquid, $[\alpha]_D -35^0$ (CHCl₃). The molecular formula was determined as C₂₂H₂₂O₇ by elementary analysis and mass spectrum [M⁺ at *m/z* 398(95%)]. The ir spectrum revealed the presence of carbonyl (1775 cm⁻¹), methylenedioxy (930 cm⁻¹), and aromatic (1585,



1499, and 1481 cm^{-1}) groups. The ^1H nmr spectrum in CDCl_3 revealed signals due to three methoxyls [δ 3.73 (6H, s) and 3.78 (3H, s)], four aromatic protons [δ 6.33 (2H, s), 6.50 and 6.64 (each 1H, s)], and methylenedioxy protons [δ 5.91 and 5.93 (each 1H, d, $J=1.3$ Hz)] as well as seven aliphatic protons [δ 2.71-2.76 (3H, m, Ha-7', H-8', H-8), 3.06 (1H, m, Hb-7'), 3.90 (1H, dd, $J=8.5, 1.6$ Hz, Ha-9), 4.42 (1H, dd, $J=8.5, 6.1$ Hz, Hb-9), and 4.58 (1H, br s, H-7)](see Table 1). As shown in Table 2, the signal pattern of the ^{13}C

Table 1. ^1H Nmr data (δ -value) for **1** (300 MHz), **2** (200 MHz)⁵, and **3** (400 MHz)⁶ (CDCl_3)

H	1	2	3
2.6	6.33 s	6.30	6.35
7	4.58 br s	4.51 d (5.1) ^a	4.36 d (3.1)
8	2.71-2.76 m	2.96 dd (13.0, 5.1)	3.36 dd (9.5, 3.1)
3,5-OMe	3.73 s	3.64 s	3.78 s
4-OMe	3.78 s	3.62 s	3.82 s
2'	6.64 s	6.80 s	6.66 s
5'	6.50 s	6.50 s	6.58 s
7'	2.71-2.76 m	2.74 dd (15.8, 11.7) 3.02 dd (15.8, 4.8)	2.47 dd (15.3, 5.4) 2.85 dd (15.3, 6.3)
8'	2.71-2.76 m	2.62 m	3.02 m
9'		3.95 dd (10.3, 8.4) 4.41 t (7.3)	3.96 dd (9.2, 3.1) 4.42 dd (9.2, 7.3)
9	3.90 dd (8.4, 3.0) 4.42 dd (8.4, 6.0)		
10'	5.91 d (1.3) 5.93 d (1.3)	5.95 s 5.96 s	5.89 d (1.4) 5.93 d (1.4)

^a Figures in parentheses are coupling constants in Hz

nmr spectrum of **1** was similar to that of deoxypodophyllotoxin (**2**)⁵ and deoxypicropodophyllotoxin (**3**)⁶ (see Table 2). But formosalactone(**1**) is different from **2** [mp 167-168 °C; $[\alpha]_D -116^0$] and **3** [mp 172-173 °C; $[\alpha]_D +27.3^0$] by comparison with their melting point, specific rotation, and nmr spectral data. From the physical data of **1** and their similarity to those of **2** and **3**, **1** can be assigned as one of eight diastereomers

Table 2. ^{13}C Nmr data (δ -value) for **1** (75 MHz), **2** (50 MHz)⁵, and **3** (100 MHz)⁶ (CDCl_3)

C	1	2	3
1	136.2	137.0	138.3
2	108.4	108.2	105.6
3	152.5	152.0	153.5
4	137.1	136.3	137.4
5	152.5	152.0	153.5
6	108.4	108.2	105.6
7	43.7	43.0	45.4
8	32.7	46.1	46.3
9	72.0	175.0	178.2
3,5-OMe	56.2	55.8	56.4
4-OMe	60.7	59.9	60.8
1'	128.3	129.1	128.4
2'	108.3	108.5	108.8
3'	147.0	146.4	147.0
4'	146.8	145.9	146.9
5'	110.5	110.0	109.8
6'	130.7	130.6	130.7
7'	33.1	32.0	32.1
8'	47.5	32.6	33.1
9'	174.9	71.5	72.8
10'	101.2	100.9	101.0

[including structures **1**, **2**, and **3**] in connection with three stereocenters and position of carbonyl.

Deoxypicropodophyllotoxin (3) can be prepared from the base-catalyzed isomerization of deoxypodophyllotoxin (2).⁷ But formosalactone (1) is stable in basic conditions, which revealed that the γ -lactone of 1 is in cis-fused. H-7 in 1 exhibited broad singlet pattern in its ¹H nmr spectrum, demonstrating that the dihedral angle between H-7 and H-8 is near 90°. Consideration of Dreiding model showed only two diastereomers (1) and (3) satisfy this requirement. In fact H-7 in 3 shows small coupling constant ($J=3.1$ Hz). Since formosalactone (1) and deoxypicropodophyllotoxin (3)⁶ are different compounds. Therefore the structure of formosalactone can be assigned as structure (1) basis on the above physical evidence.

Formosalactone (1) was reduced with lithium aluminium hydride to afford a diol (4) [mp 234-237 °C; ν cm⁻¹ 3395; δ 3.40-3.81 (4H, m, H-9, H-9')], which was also identified with the product from deoxypicropodophyllotoxin (3) by lithium aluminium hydride reduction.⁷ Thus, formosalactone was confirmed to be the isomer of deoxypicropodophyllotoxin concerning the position of lactone carbonyl. The stereostructure of 1 derived on the basis of NOE experiments is shown in structure (5).

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 781 spectrometer. ¹H and ¹³C nmr spectra run on a Bruker AM 300 at 300 MHz in CDCl₃ solution with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given in δ -value and coupling constants (J) are given in hertz (Hz). EI-ms was taken on a JEOL-JMS-100 spectrometer.

Extraction and Isolation

The bark of *J. formosana* Hay. var. concolor Hay. (980 g) was extracted with methanol (20 l) five times (4 days for every time) at room temperature. The combined extracts were evaporated *in vacuo* to give a residue (48 g), which was subsequently subjected to chromatography on silica gel with gradient (hexane-ethyl acetate) system. Savinin (10 mg)⁴ and formosalactone (1) (12 mg) were eluted with solvent system 20% ethyl acetate in hexane and 30% ethyl acetate in hexane, respectively.

Formosalactone (1) : light yellow liquid; $[\alpha]_D^{25} -35.0$ (c 0.3 in CHCl_3); ir (neat) ($\nu \text{ cm}^{-1}$) 1775, 1585, 1499, 1481, 1415, 1331, 1287, 1224, 1126; ms m/z (%) 398 (M^+ , 95), 230 (20), 185 (57), 181 (100), 173 (80), 168(37), 153(27); Anal. Calcd for $\text{C}_{22}\text{H}_{22}\text{O}_7$: C, 66.32; H, 5.57. Found C, 66.47; H 5.59.

Reduction of 1 by Lithium Aluminium Hydride

LiAlH_4 (50 mg, 1.3 mmol) was added to a solution of formosalactone (1) (8 mg, 0.02 mmol) in dry THF (10 ml) and the reaction mixture was left at room temperature for 1 h. The reaction mixture was quenched with 0.05 ml of water. 10% NaOH (0.05 ml) of aqueous solution was subsequently poured into the reaction mixture and stirred for 5 min. Then 0.1 ml of water was added and the reaction mixture was stirred until to the white precipitation appearance. After filtering, the filtrate was purified on silica gel chromatography (30% ethyl acetate in hexane) to yield diol (2) (6 mg) [mp 234-237 $^{\circ}\text{C}$ (lit.,⁷ 232-236 $^{\circ}\text{C}$); $[\alpha]_D -34.1$ (c 0.5 in CHCl_3); ir (KBr) ($\nu \text{ cm}^{-1}$) 3395, 1585, 1498, 1480, 1416, 1322, 1226, 1183, 1126, 1037, 1006, 937, 850, 816; ^1H nmr (CDCl_3) δ 2.01-2.07(2H, m, H-8, H-8'), 2.65-2.84 (2H, m, H-7'), 3.40-3.81 (4H, m, H-9, H-9'), 3.72, 3.72, 3.77 (each 3H, s), 4.06 (1H, d, $J=3.2$ Hz, H-7), 5.83 (2H, s, H-10'), 6.20 (2H, s), and 6.33 and 6.58 (each 1H, s).

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