Phytochemistry, Vol. 28, No. 3, pp. 952 954, 1989.
Printed in Great Britain.

0031-9422/89 $3.00 + 0.00

A LIGNAN FROM *ACTINODAPHNE LONGIFOLIA*

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(*Received* 12 *July* 1988)

Key Word Index—*Actinodaphne longifolia*; Lauraceae; lignan; actifolin; piperitol.

Abstract—A new lignan, actifolin, was isolated from the leaves of *Actinodaphne longifolia* and the structure was established on the basis of chemical and spectroscopic evidence.

INTRODUCTION

Previously, Hayashi and co-workers [1] reported the isolation of two furanosesquiterpenes (sesquirosefuran and longifolin) from the leaves of *Actinodaphne longifolia* (Blume) Nakai (Lauraceae), which grows in the southern part of Japan. In the course of our further investigation of the fresh leaves of this plant, three lignans (**1**, **8**, and **9**) were isolated and one of them was a new compound. We now wish to describe the isolation and characterization of this compound (**1**).

RESULTS AND DISCUSSION

The new compound, actifolin (**1**), $C_{22}H_{24}O_7$, gave a brown colour with ethanolic ferric chloride and exhibited the presence of hydroxy group (3550 cm^{-1}) and ester group (1735 cm^{-1}) in the IR spectrum. Acetylation of actifolin with acetic anhydride and pyridine gave a diacetate (**2**). The ^1H NMR spectrum of actifolin displayed the presence of six aromatic protons in a complicated pattern at δ 6.64–6.85 (6H, *m*), a methylenedioxy group at δ 5.94 (2H, *s*), a hydroxy group at δ 5.51 (1H, *s*), a methoxy group at δ 3.88 (3H, *s*), and an acetyl group at δ 2.03 (3H, *s*). The remaining nine protons were found in the region between δ 4.8 and 2.5 (see Experimental). In the ^{13}C NMR spectra, all the signals for compound **1** were very similar to those of piperitol (**8**), isolated from the same plant, except for the signals of C-8, C-9, C-7′, and C-8′ (Table 1). These data suggested that actifolin would be a seco-derivative of **8**. As the mass spectrum of actifolin showed the greater abundance of the fragmentation peak at *m/z* 137, the structure of this compound must be **1** and therefore the alternative structure **4** was ruled out [2].

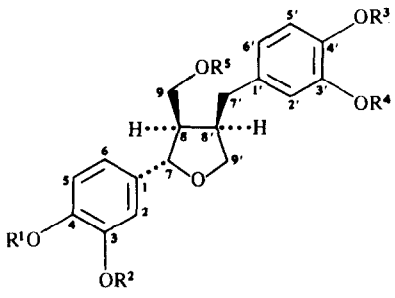
The stereochemistry of **1** was determined as follows. Two compounds, **6** (*trans*-orientation between 7-H and 8-H) and **7** (*cis*-orientation between 7-H and 8-H), were prepared by hydrogenolysis of eudesmin (**10**) [3] and epieudesmin (**11**) [3], respectively. In the ^1H NMR spectra, the signal of 7-H in **6** (*trans*-isomer) was observed at δ 4.82, against that in **7** (*cis*-isomer) at δ 5.13. The corresponding signal in the spectrum of **1** was observed at δ 4.76, which agrees well with the assignment of the *trans*-orientation between 7-H and 8-H.

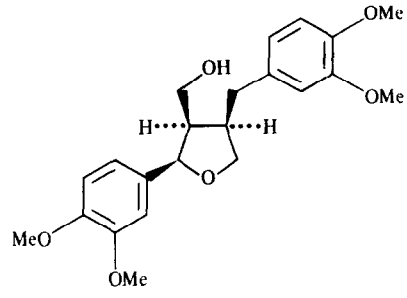
In order to confirm the structure of **1**, a chemical study was also carried out. Hydrolysis of **1** afforded an alcohol (**3**). Hydrogenolysis of piperitol (**8**), with known stereochemistry, gave a mixture of alcohols, **3** and **5**. Separation of the mixture by HPLC afforded **3**, which was identical with the hydrolysis product of **1**. Thus, the structure of actifolin is established to be **1**.

In addition to the new compound, actifolin (**1**), two known lignans piperitol (**8**) [4] and sesamin (**9**) were isolated and identified from this plant. This is the first report of lignans isolated from the genus *Actinodaphne*.

Table. 1. ^{13}C NMR spectral data of compounds **1** and **8**

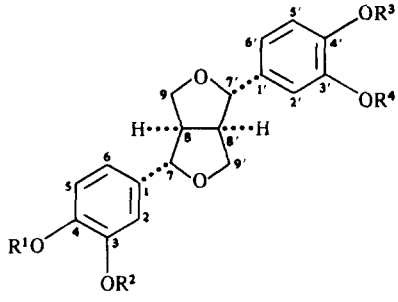
C	**1**	**8**
1	136.5 *s*	135.1 *s*
2	106.2 *d*	106.5 *d*
3	147.8 *s*	148.0 *s*
4	146.5 *s*	146.8 *s*
5	108.1 *d*	108.2 *d*
6	119.2 *d*	119.3 *d*
7	83.1 *d*	85.9 *d*
8	49.1 *d*	54.3 *d*
9	62.7 *t*	71.7 *t*
1′	131.8 *s*	132.9 *s*
2′	111.2 *d*	108.7 *d*
3′	147.0 *s*	147.1 *s*
4′	144.1 *s*	145.3 *s*
5′	114.5 *d*	114.4 *d*
6′	121.1 *d*	119.0 *d*
7′	33.2 *t*	85.9 *d*
8′	42.5 *d*	54.2 *d*
9′	72.8 *t*	71.7 *t*
OMe	55.9 *q*	56.0 *q*
OCH_2O	101.0 *t*	101.1 *t*
C=O	170.9 *s*	—
Me	20.1 *q*	—

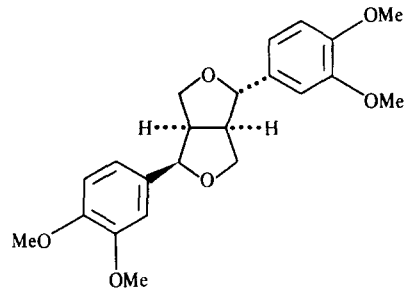




1 $R^1 + R^2 =$ —CH_2—, $R^3 = H$, $R^4 = Me$, $R^5 = Ac$
2 $R^1 + R^2 =$ —CH_2—, $R^3 = R^5 = Ac$, $R^4 = Me$
3 $R^1 + R^2 =$ —CH_2—, $R^3 = R^5 = H$, $R^4 = Me$
4 $R^1 = H$, $R^2 = Me$, $R^3 + R^4 =$ —CH_2—, $R^5 = Ac$
5 $R^1 = R^5 = H$, $R^2 = Me$, $R^3 + R^4 =$ —CH_2—
6 $R^1 = R^2 = R^3 = R^4 = Me$, $R^5 = H$

7





8 $R^1 + R^2 =$ —CH_2—, $R^3 = H$, $R^4 = Me$
9 $R^1 + R^2 = R^3 + R^4 =$ —CH_2—
10 $R^1 = R^2 = R^3 = R^4 = Me$

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EXPERIMENTAL

CC was run on Merck silica gel 60 (230–400 mesh) and florisil (100–200 mesh). TLC was performed on glass plates precoated with Kieselgel 60 F_{254} (Merck). ^{1}H NMR (270 MHz) and ^{13}C NMR (25 MHz) spectra were determined in $CDCl_3$. Chemical shifts are in ppm (δ). HPLC was conducted on a Develosil pack (ODS-10) column (20 × 250 mm) with UV detector (254 nm).

Extraction and separation of compounds. The MeOH extract of the fresh leaves (6.0 kg) of *Actinodaphne longifolia* collected in Kagoshima prefecture in August 1987 was divided into the *n*-hexane soluble (150 g) and $CHCl_3$ soluble fractions (32 g). The *n*-hexane soluble fraction was chromatographed on florisil with C_6H_6 as an eluent to give sesquirosefuran (1.3 g) and longifolin (7.7 g). The $CHCl_3$ soluble fraction was chromatographed on florisil. Elution with $CHCl_3$ afforded an oil (3.7 g), a part of which (0.7 g) was chromatographed on silica gel to yield sesamin (**9**) (8 mg). Further elution with $CHCl_3$–Me_2CO (9:1) afforded an oil (1.8 g) which was subjected by CC on silica gel ($CHCl_3$–Me_2CO, 19:1) and successively by prep. TLC ($CHCl_3$–Me_2CO, 9:1) providing piperitol (**8**) (37 mg) and actifolin (**1**) (24 mg).

Actifolin (**1**). Colourless oil. $[\alpha]_D + 13.3°$ ($CHCl_3$; *c* 0.48). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1735, 1610, 1515. UV λ_{max}^{EtOH} nm: 231. MS *m/z*: 400 $[M]^+$, 357, 340, 217, 203, 190, 176, 164, 149, 137. HRMS *m/z*: 400.1516 (M^+, calcd for $C_{22}H_{24}O_7$: 400.1522). ^{1}H NMR ($CDCl_3$): δ 2.03 (3H, *s*, COMe), 2.51 (1H, *dd*, *J* = 13.1, 9.8 Hz, 7′-H), 2.51 (1H, *d*, *J* = 6.7 Hz, 8-H), 2.67–2.76 (1H, *m*, 8′-H), 2.82 (1H, *dd*, *J* = 13.1, 5.0 Hz, 7′-H), 3.72 (1H, *dd*, *J* = 8.7, 6.7 Hz, 9′-H), 3.88 (3H, *s*, OMe), 4.05 (1H, *dd*, *J* = 8.7, 6.7 Hz, 9′-H), 4.16 (1H, *dd*, *J* = 11.4, 7.7 Hz, 9-H), 4.34 (1H, *dd*, *J* = 11.4,7.1 Hz, 9-H), 4.76 (1H, *d*, *J* = 6.1 Hz, 7-H) 5.51 (1H, *s*, OH), 5.94 (2H, *s*, OCH_2O), 6.64–6.85 (6H, *m*, arom. H).

Acetylation of actifolin. A mixture of **1** (2 mg), Ac_2O (0.5 ml), and pyridine (0.5 ml) was stirred overnight at room temp. and worked up in the usual way to afford a colourless oil (**2**, 2 mg). $[\alpha]_D + 23.0°$ ($CHCl_3$; *c* 0.10). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1740, 1605, 1510. UV λ_{max}^{EtOH} nm: 279, 227. MS *m/z*: 442 $[M]^+$, 400, 382, 340, 203, 149, 137. HRMS *m/z*: 442.1647 (M^+, calcd for $C_{24}H_{26}O_8$: 442.1626). ^{1}H NMR ($CDCl_3$): δ 2.03 (3H, *s*, COMe), 2.31 (3H, *s*, COMe), 2.52 (1H, *m*, 8-H), 2.56 (1H, *dd*, *J* = 13.1, 10.4 Hz, 7′-H), 2.68–2.81 (1H, *m*, 8′-H), 2.87 (1H, *dd*, *J* = 13.1, 5.0 Hz, 7′-H), 3.74 (1H, *dd*, *J* = 8.4, 6.4 Hz, 9′-H), 3.82 (3H, *s*, OMe), 4.08 (1H, *dd*, *J* = 8.4, 6.4 Hz, 9′-H), 4.17 (1H, *dd*, *J* = 11.4, 7.4 Hz, 9-H), 4.34 (1H, *dd*, *J* = 11.4, 7.4 Hz, 9-H), 4.77 (1H, *d*, *J* = 6.4 Hz, 7-H), 5.95 (2H, *s*, OCH_2O), 6.72–6.97 (6H, *m*, arom. H).

Hydrogenolysis of eudesmin. A suspension of eudesmin (**10**) (12 mg) and 5% Pd-C (12 mg) in MeOH (1 ml) was stirred under a hydrogen atmosphere at room temp. for 7.5 hr. The reaction mixture was filtered and the filtrate was evapd. The residue was purified by prep. TLC ($CHCl_3$–Me_2CO, 9:1) to afford a colourless oil (**6**, 3.1 mg). $[\alpha]_D + 14.7°$ ($CHCl_3$; *c* 0.08). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1515, 1465. MS *m/z*: 388 $[M]^+$, 151. ^{1}H NMR ($CDCl_3$): δ 2.43

(1H, *quint.*, $J = 6.7$ Hz, 8-H), 2.58 (1H, *dd*, $J = 13.5$, 10.6 Hz, 7′-H), 2.72–2.80 (1H, *m*, 8′-H), 2.94 (1H, *dd*, $J = 13.5$, 5.2 Hz, 7′-H), 3.76 (1H, *dd*, $J = 8.7$, 6.7 Hz, 9′-H), 3.80–3.89 (1H, *dd*, $J = 10.6$, 6.7 Hz, 9-H), 3.86, 3.87, 3.89 (12H, 3 × *s*, 4 × OMe), 3.94 (1H, *dd*, $J = 10.6$, 6.7 Hz, 9-H), 4.07 (1H, *dd*, $J = 8.7$, 6.4 Hz, 9′-H), 4.82 (1H, *d*, $J = 6.7$ Hz, 7-H), 6.71–6.89 (6H, *m*, arom. H).

Hydrogenolysis of epieudesmin. Epieudesmin (**11**) (11 mg) in MeOH (1 ml) and 5% Pd-C (11 mg) was hydrogenated at room temp. for 13.5 hr according to the method described above. Purification of the reaction product by prep. TLC ($CHCl_3$–Me_2CO, 9:1)afforded a colourless oil (**7**, 1.7 mg). $[\alpha]_D$ +45.7° ($CHCl_3$, *c* 0.04). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1515, 1465. MS *m/z*: 388 $[M]^+$, 151. ^1H NMR ($CDCl_3$): δ 2.40–2.48 (1H, *m*, 8-H), 2.78 (1H, *dd*, $J = 11.1$, 4.6 Hz, 7′-H), 2.90–2.99 (2H, *m*, 7′-H and 8′-H), 3.54 (1H, *dd*, $J = 12.1$, 4.0 Hz, 9-H), 3.63 (1H, *dd*, $J = 12.1$, 5.4 Hz, 9-H), 3.87, 3.89 (12H, 2 × *s*, 4 × OMe), 3.83–3.91 (1H, *m*, 9′-H), 4.03 (1H, *t*, $J = 8.1$ Hz, 9′-H), 5.13 (1H, *d*, $J = 5.4$ Hz, 7-H), 6.76–6.95 (6H, *m*, arom. H).

Hydrolysis of actifolin. A soln of **1** (2.3 mg) and 3% aq NaOH (3 drops) in MeOH (0.5 ml) was stirred at room temp. for 10 min. After removal of solvent, the residue was diluted with H_2O, neutralized with dil. HCl, and extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and evapd to dryness to give a colourless oil (**3**, 2.0 mg). $[\alpha]_D$ +11.1° ($CHCl_3$, *c* 0.09). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3530, 1610, 1510. UV λ_{max}^{EtOH} nm: 283, 230. MS *m/z*: 358 $[M]^+$, 137. HRMS *m/z*: 358.1389 (M^+, calcd for $C_{20}H_{22}O_6$: 358.1415). ^1H NMR ($CDCl_3$): δ 2.37 (1H, *quint.*, $J = 6.7$ Hz, 8-H), 2.54 (1H, *dd*, $J = 13.1$, 10.7 Hz, 7′-H), 2.72 (1H, *m*, 8′-H), 2.90 (1H, *dd*, $J = 13.1$, 5.0 Hz, 7′-H), 3.75 (1H, *dd*, $J = 8.7$, 6.1 Hz, 9′-H), 3.77 (1H, *dd*, $J = 10.7$, 6.7 Hz, 9-H), 3.88 (3H, *s*, OMe), 3.92 (1H, *dd*, $J = 10.7$, 6.7 Hz, 9-H), 4.05 (1H, *dd*, $J = 8.7$, 6.7 Hz, 9′-H), 4.78 (1H, *d*, $J = 6.7$ Hz, 7-H), 5.49 (1H, *s*, OH), 5.95 (2H, *s*, OCH_2O), 6.68–6.86 (6H, *m*, arom. H).

Hydrogenolysis of piperitol. Piperitol (**8**) (10 mg) in MeOH (1 ml) and 5% Pd-C (10 mg) was hydrogenated at room temp. for 30 hr as already described above. Treatment of the reaction mixture in the usual way afforded a mixture of alcohols (**3** and **5**). The mixture was separated by HPLC (MeOH–H_2O, 1:1; flow rate 9.0 ml) to give **3** (0.6 mg) at R_t 31 min. and **5** (1.5 mg) at R_t 37 min. The alcohol (**3**) was identical with the product obtained by hydrolysis of **1**. Compound **5** was a colourless oil. $[\alpha]_D$ +6.0° ($CHCl_3$; *c* 0.06). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3530, 1600, 1510, 1500. UV λ_{max}^{EtOH} nm: 283, 230. MS *m/z*: 358 $[M]^+$, 135. HRMS *m/z*: 358.1427 (M^+, calcd for $C_{20}H_{22}O_6$: 358.1415). ^1H NMR ($CDCl_3$): δ 2.40 (1H, *quint.*, $J = 6.7$ Hz, 8-H), 2.55 (1H, *dd*, $J = 13.4$, 10.4 Hz, 7′-H), 2.65–2.76 (1H, *m*, 8′-H), 2.90 (1H, *dd*, $J = 13.4$, 5.0 Hz, 7′-H), 3.72 (1H, *dd*, $J = 8.7$, 6.4 Hz, 9′-H), 3.77 (1H, *dd*, $J = 10.7$, 6.7 Hz, 9-H), 3.90 (3H, *s*, OMe), 3.91 (1H, *dd*, $J = 10.7$, 6.7 Hz, 9-H), 4.06 (1H, *dd*, $J = 8.7$, 6.4 Hz, 9′-H), 4.79 (1H, *d*, $J = 6.7$ Hz, 7-H), 5.51 (1H, *br s*, OH), 5.93 (2H, *s*, OCH_2O), 6.62–6.89 (6H, *m*, arom. H).

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