Pergamon

Phytochemistry, Vol. 46, No. 7, pp. 1283–1284, 1997

Printed in Great Britain
0031-9422/97 $17.00+0.00

PII: S0031-9422(97)00452-4

BISESQUITERPENOID FROM THE ROOT OF *LINDERA STRYCHNIFOLIA*

ISAO KOUNO,* ASUKA HIRAI, ZHI-HONG JIANG and TAKASHI TANAKA

Faculty of Pharmaceutical Sciences, Nagasaki University, Bunkyo-machi 1-14, Nagasaki 852, Japan

(*Received in revised form* 28 *April* 1997)

Key Word Index—*Lindera strychnifolia*; Lauraceae; sesquiterpene; lindestenolide; bilindestenolide.

Abstract—From the root of *Lindera strychnifolia*, which is well known to contain many kinds of sesquiterpenes, a new bisesquiterpene has been isolated. The structure of this compound was elucidated by spectroscopic analysis, including COSY, HMBC and HMQC techniques. © 1997 Published by Elsevier Science Ltd

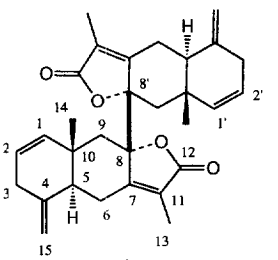
INTRODUCTION

The root of *Lindera strychnifolia* Vill. has a strong fragrance, and is used in Chinese folk medicine as a palliative and an antispasmodic. In previous studies of the constituents from this plant, about 20 eudesmanes and elemanes were isolated [1, 2]. As part of our chemical studies of novel sesquiterpenes from natural medicines, a new bisesquiterpene has been isolated from the root of *L. strychnifolia*. This type of structure has just been reported for sesquiterpenes isolated from the branches of the herbal plant, *Atractylodes macrocephala* (Compositae) [3].

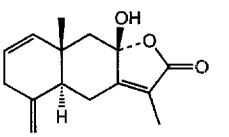
RESULTS AND DISCUSSION

The roots of *L. strychnifolia* were extracted successively with Et_2O and MeOH. The Et_2O extract and the Et_2O and EtOAc soluble portions of the MeOH extract were combined and worked up by standard procedures to give compound **1** along with four known sesquiterpenes, linderalactone [4], linderane [5], neolinderane [6] and hydroxylindestenolide (**2**) [7].

The ^{13}C NMR spectrum of **1** contained 15 signals which were assigned to two methyls, three methylenes, one methine, six sp^2, two quaternary and one carbonyl carbons. Thus, compound **1** appeared to be formed from two identical units. The ^{13}C signals, together with the EI-mass spectral data ($[M]^+ = m/z$ 458) led to the molecular formula of $C_{30}H_{34}O_4$ for **1**. Its IR, spectrum exhibited strong γ-lactone absorption at 1742 cm^{-1}. In the ^{13}C NMR spectrum, the signal at δ_C 171.9 supported the presence of a γ-lactone group.



1



2

The ^1H and ^{13}C NMR spectra showed the signals of one terminal double bond at δ_H 4.38 and 4.99 (δ_C 108.1), and two methyl groups at δ_H 1.21 and 1.77 (δ_C 21.1 and 8.6). The strong resemblance of these features, particularly the ^{13}C signals, to those of hydroxylindestenolide (**2**) indicated that one unit of **1** was dehydroxy-hydroxylindestenolide. However, the signal at δ_C 103.8 of **2** was replaced in **1** with a signal of δ_C 89.3 (C-8). Although we did not isolate lindestenolide [7], and could not compare its ^{13}C NMR signals with those of **1**, the COSY, HMQC and HMBC spectra unambiguously supported the above unit. Therefore, the structure of **1** was elucidated as the *bis* form of lindestenolide linked at the C-8 position.

The stereochemistry of H-5 and CH_3-14 was assigned by the NOE experiment. When the CH_3-14 signal at δ_H 1.21 was irradiated, NOE enhancements of the signals of H-9b, H-6b and H-1, but not H-5, were observed. The coupling constants of H-5 and H-6b (13.3 Hz) and H-5 and H-6a (3.2 Hz) suggested that both H-5 and H-6b were axial hydrogens. These results established the *trans* relationship of H-5 and CH_3-14.

Very recently, biatractylolide having the above type of structure was isolated from the Chinese herbal plant *Atractylodes macrocephala* [3]. Biatractylolide is a

* Author to whom correspondence should be addressed.

Table 1. ^{13}C NMR data of compound **2** and ^{1}H and ^{13}C NMR data of compound **1** ($CDCl_3$)

	2*		**1**	
Position	C	Position	C	H
1	137.4	1,1′	137.6	5.60 (*dt*, *J* = 9.7, 1.2 Hz)
2	122.7	2,2′	123.1	5.49 (*dt*, *J* = 9.7, 3.4 Hz)
3a	34.6	3a,3a′	34.7	2.78 (*m*)
3b		3b,3b′		2.82 (*m*)
4	145.2	4,4′	144.7	
5	49.7	5,5′	51.3	2.06 (*dd*, *J* = 13.3, 3.2 Hz)
6a	23.9	6a,6a′	27.4	2.76 (*dd*, *J* = 13.3 3.2 Hz)
6b		6b,6b′		2.88 (*br t*, *J* = 13.3 Hz)
7	161.2	7,7′	164.3	
8	103.8	8,8′	89.3	
9a	47.9	9a,9a′	46.8	1.57 (*d*, *J* = 14.7 Hz)
9b		9b,9b′		2.90 (*d*, *J* = 14.7 Hz)
10	37.5	10,10′	38.1	
11	121.8	11,11′	124.8	
12	172.6	12,12′	171.9	
13	8.1	13,13′	8.6	1.77 (*s*)
14	20.1	14,14′	21.1	1.21 (*s*)
15a	107.2	15a,15a′	108.1	4.83 (*s*)
15b		15b,15b′		4.99 (*s*)

* These data are almost the same as those of reference [7].

1,1′,2,2′-tetrahydro derivative of compound **1**. The stereochemistry at C-8 of **1** was thought to be the same as biatractolide, because the proton chemical shifts of H-9b of both compounds were similar to each other. This signal appeared exclusively at low field at δ_H 2.90 and was probably affected by the ether–oxygen of the γ-lactone moiety. Such an arrangement is possible when the stereostructure at C-8 has the β-configuration. This hypothesis was supported by the structural model generated by means of the CAChe work system [8].

EXPERIMENTAL

General. NMR: 500 MHz (^{1}H) and 125 MHz (^{13}C), $CDCl_3$ with TMS at int. standard. ^{1}H-^{1}H COSY, HMQC and HMBC were performed using a gradient technique.

Plant material. The roots of *L. strychnifolia* were collected in the autumn of 1995 in the Botanical Garden, Nagasaki University, and identified by Dr Toshihiko Ikenaga (Assoc. Prof. of the Botanical Garden).

Extraction and isolation. The roots (2.9 kg) were extracted ×3 with Et_2O, then ×3 with MeOH. The Et_2O extract was evapd. *in vacuo* to give a residue (53.7 g). The Et_2O (33.3 g)- and EtOAc (0.37 g)-soluble portions of the MeOH extracts were combined with the Et_2O extract. The combined residual part was suspended in C_6H_6 to give a supernatant, which was evapd *in vacuo* to give a residue (42.2 g). This was chromatographed over silica gel using C_6H_6–MeOH (19:1) as the solvent system. Successive CC on silica gel with *n*-hexane–EtOAc (19:1) afforded the sesquiterpenes linderalactone (400.0 mg), linderane (605.4 mg), neolinderane (80.5 mg) and hydroxylindestenolide (37.8 mg) together with compound **1** (bilindestenolide) (3.2 mg). All these compounds were crystallized from *n*-hexane–EtOAc. Known compounds were identified by comparison their mps and spectroscopic data with those in the literature.

Bilindestenolide (**1**). Mp 300°>. $[\alpha]_D^{15}$ +201.7° ($CHCl_3$; *c* 0.2). IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1742 (γ-lactone), 1673 and 1652; EI-MS; *m/z* 458 $[M]^+$; ^{1}H and ^{13}C NMR: Table 1.

REFERENCES

1. Takeda, K., Horibe, I. and Minato, H., *Journal of the Chemical Society*, (*C*), 1968, 569.
2. Tada, H., Minato, H. and Takeda, K., *Journal of the Chemical Society*, 1971, 1070, and references cited therein.
3. Lin, Y.-C., Jin, T., Wu, X.-Y., Huang, Z.-Q. and Fan, J.-S., *Journal of Natural Products*, 1997, **60**, 27.
4. Takeda, K., Minato, H. and Ishikawa, M., *Journal of the Chemical Society*, 1964, 4578.
5. Takeda, K., Minato, H. and Horibe, I., *Tetrahedron*, 1963, **19**, 2307.
6. Joshi, B. S., Kamat, V. N. and Govindachari, T. R., *Tetrahedron*, 1967, **23**, 267.
7. Takeda, K., Horibe, I. and Minato, H., *Journal of the Chemical Society*, 1968, 569.
8. CAChe Scientific, Inc. Version 3.7.