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LIGNANS FROM *MACHILUS THUNBERGII*

HIROKO SHIMOMURA, YUTAKA SASHIDA and MOTOMU OOHARA

Tokyo College of Pharmacy, 1432-1, Horinouchi, Hachioji, Tokyo 192-03, Japan

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Key Word Index—*Machilus thunbergii*; Lauraceae; 2,5-diaryl-3,4-dimethyltetrahydrofuran type neolignans; machilin-F, G, H, I; (−)-nectandrin-A.

Abstract—Five new neolignans, machilin-F [2-(4-hydroxy-3-methoxyphenyl)-3,4-dimethyl-5-piperonyltetrahydrofuran], machilin-G [2-(3,4-dimethoxyphenyl)-3,4-dimethyl-5-piperonyltetrahydrofuran], machilin-H [2-(4-hydroxy-3,5-dimethoxyphenyl)-3,4-dimethyl-5-(4-hydroxy-3-methoxyphenyl)tetrahydrofuran], machilin-I [2,5-bis-(4-hydroxy-3-methoxyphenyl)-3,4-dimethyltetrahydrofuran], (−)-nectandrin-A and the known compound, nectandrin-B were isolated from the bark of *Machilus thunbergii* and their structure were determined.

INTRODUCTION

In a previous paper [1], we reported the isolation of the neolignans, machilin-A–E, from the bark of *Machilus thunbergii* Sieb. et Zucc. The methanol extract of the bark of this palnt was further investigated and 2,5-diaryl-3,4-dimethyltetrahydrofuran type neolignans, machilin-F–I, were isolated we now report their structures elucidated by means of spectral analysis.

RESULTS AND DISCUSSION

Machilin-F (**1**) was obtained as a colourless oil. In the EI-mass spectrum, a molecular ion peak was observed at m/z 342. The ^{1}H NMR and IR spectra indicated that **1** was a diastereomer of austrobailignan-7 [2] and chicanine [3] belonging to the 2,5-diaryl-3,4-dimethyltetrahydrofuran type of neolignans.

The chemical shifts of H-2 (δ4.44), H-5 (4.46) and 3,4-Me (1.01) in the ^{1}H NMR spectrum indicated each methyl group to be situated in a *trans*-relation to the vicinal aryl group [4, 5]. The configuration of **1** was thus concluded to be either the all *trans* form or the *meso* form and the chemical shifts of H-3 and H-4 (δ2.19) indicated the 3,4-*cis*-relationship [6]. Furthermore, compound **1** showed no Cotton effect (200–350 nm), but known compounds of the all *trans*-configuration did so in circular dichroism [7]. Thus, the configuration for the structure of **1** was found to be the *meso*-configuration with the 3-Me and 4-Me groups situated in a *cis*-relationship to each other. From these data, the structure of **1** is thus shown to be (2*R**, 3*R**, 4*S**, 5*R**)-2-(4-hydroxy-3-methoxyphenyl)-3,4-dimethyl-5-piperonyltetrahydrofuran.

Compounds **2**–**5** were each obtained as a colourless oil. From the ^{1}H and ^{13}C NMR spectral data, these compounds may also possibly be derivatives of the 2,5-diaryl-3,4-dimethyltetrahydrofuran type of neolignan. Their relative configurations were shown to be the same as that of **1** by the ^{1}H NMR, specific rotation and circular dichroism data.

Machilin-G (**2**) showed a molecular ion peak at m/z 356 in the EI-mass spectrum, and its IR spectrum showed no absorption band for a hydroxyl group. The above data and ^{1}H NMR spectrum indicated **2** to be (2*R**, 3*R**, 4*S**, 5*R**)-2-(3,4-dimethoxyphenyl)-3,4-dimethyl-5-piperonyltetrahydrofuran, a diasteromer of calopiptin [6, 8].

Compounds **3** and **4** were identified as nectandrin-B and an enantiomer of nectandrin-A, respectively, by comparison with data in the literature [9].

Machilin-H (**5**) showed absorption band(s) of hydroxyl group(s) in its IR spectrum. A molecular ion peak was noted at m/z 374 in the EI-mass spectrum. The ^{1}H NMR and ^{13}C NMR spectra indicated the structure of **5** to possibly be (2*R**, 3*R**, 4*S**, 5*R**)-2-(4-hydroxy-3,5-dimethoxyphenyl)-3,4-dimethyl-5-(4-hydroxy-3-methoxyphenyl) tetrahydrofuran.

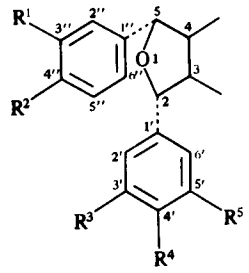
Machilin-I (**6**) was obtained as a colourless oil. From the IR, ^{1}H NMR and EI-mass spectral data, it was concluded to be a diastereomer of nectandrin-B. The signals of methine (δ5.45) and methyl groups (0.61) due to H-2 and 3-Me, respectively, of this compound shifted further downfield and upfield than those of **1** by the anisotropic effect of the aromatic group at C-2 [4, 5]. The methyl group at C-3 thus appears to be in a *cis*-relationship to the aromatic group at C-2. By measuring the NOE-correlated 2D NMR spectrum of **6**, the *cis*-configuration between the methyl groups at C-3 and C-4 was established. The relative configuration of this compound may thus be represented as (2*S**, 3*R**, 4*S**, 5*R**)-2,5-bis-(4-hydroxy-3-methoxyphenyl)-3,4-dimethyltetrahydrofuran.

Compounds **1**, **2**, **4**–**6** have not been reported previously as naturally occurring lignans.

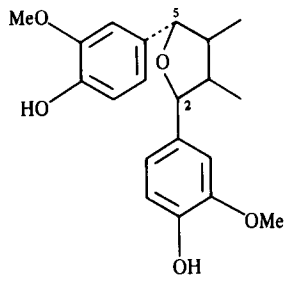
EXPERIMENTAL

NMR spectra were measured at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. Chemical shifts were given on the (ppm) scale with TMS as the internal standard. Details of the extraction and isolation are described in the previous paper [1].

Machilin-G (**2**). Colourless oil, 15.3 mg; $[\alpha]_D^{24°}$ 10.8° ($CHCl_3$; *c* 0.40); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 2930, 1710, 1450, 1230; UV λ_{max}^{EtOH} nm (log ε): 282 (3.63), 231 (3.93), 208 (4.24); ^{1}H NMR ($CDCl_3$): δ 1.01 (6H, *d*, *J* = 6.7 Hz, 3,4-Me), 2.29 (2H, *m*, H-3,4), 4.44 (1H, *d*, *J* = 6.3, Hz, H-2 or 5), 4.46 (1H, *d*, *J* = 6.7 Hz, H-2 or



	R^1	R^2	R^3	R^4	R^5
1	OCH_2O		OMe	OH	H
2	OCH_2O		OMe	OMe	H
3	OMe	OH	OMe	OH	H
4	OMe	OH	OMe	OMe	H
5	OMe	OH	OMe	OH	OMe



6

5), 3.90 (3H, *s*, –OMe), 5.95 (2H, *s*, OCH_2O), 6.76–6.97 (6H, *m*, aromatic protons); MS (*m/z*): 342 $[M]^+$, 190, 175, 145.

Machilin-G (**2**): Colourless oil, 15.3 mg; $[\alpha]_D^{24°}$ 3.9° ($CHCl_3$; *c* 0.30); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2960, 1595, 1518, 1263; UV λ_{max}^{EtOH} nm (log ε): 282 (4.19), 217 (4.45); ^1H NMR ($CDCl_3$): δ 1.02 (3H, *d*, *J* = 6.7 Hz, 3 or 4-Me), 1.03 (3H, *d*, *J* = 6.7 Hz, 3 or 4-Me), 2.30 (2H, *m*, H-3,4), 3.88 (3H, *s*, OMe), 3.90 (3H, *s*, OMe), 4.46 (1H, *d*, *J* = 6.9 Hz, H-2 or 5), 4.47 (1H, *d*, *J* = 6.9 Hz, H-2 or 5), 5.95 (2H, *s*, OCH_2O), 6.80–6.99 (6H, *m*, Ar-H); MS (*m/z*): 356 $[M]^+$, 340, 206, 190, 175, 145.

Nectandrin-B (**3**). Colourless oil, 448 mg; $[\alpha]_D^{23°}$ 0° ($CHCl_3$; *c* 0.40)

(−)-*Nectandrin-A* (**4**). Colourless oil, 80 mg; $[\alpha]_D^{23°}$ −8.9° ($CHCl_3$; *c* 0.40); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2950, 1605, 1250; UV λ_{max}^{EtOH} nm (log ε): 279 (3.92), 230 (4.30), 210 (4.35); ^1H NMR ($CDCl_3$): δ 1.05 (3H, *d*, *J* = 6.7 Hz, 3 or 4-Me), 1.04 (3H, *d*, *J* = 6.7 Hz, 3 or 4-Me), 2.30 (2H, *m*, H-3,4), 3.90 (9H, *s*, OMe), 4.50 (1H, *d*, *J* = 6.2 Hz, H-2 or 5), 4.51 (1H, *d*, *J* = 6.2 Hz, H-2 or 5), 5.55 (1H, *br*, OH), 6.80–7.00 (6H, *m*, Ar-H); MS (*m/z*): 358 $[M]^+$, 216, 192, 145.

Machilin-H (**5**). Colourless oil, 7.3 mg; $[\alpha]_D^{25°}$ 8.8° ($CHCl_3$; *c* 0.37); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 2930, 1610, 1510, 1460, 1210; UV λ_{max}^{EtOH} nm (log ε): 279 (3.91), 216 (4.38); ^1H NMR ($CDCl_3$): δ 1.05 (6H, *d*, *J* = 6.8 Hz, 3, 4-Me), 2.35 (2H, *m*, H-3,4), 3.90 (9H, *s*, OMe), 4.49 (1H, *d*, *J* = 5.3 Hz, H-2 or 5), 4.50 (1H, *d*, *J* = 5.3 Hz, H-2 or 5), 5.47 (1H, *br*, OH), 5.58 (1H, *br*, OH), 6.65 (2H, *s*, Ar-H), 6.91 – 6.96 (3H, *m* Ar-H); MS (*m/z*): 374 $[M]^+$, 222, 192, 145.

Machilin-I (**6**). Colourless oil, 2.6 mg; $[\alpha]_D^{25°}$ −93.0° ($CHCl_3$; *c* 0.13); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 2920, 1500, 1450, 1260, 1200; UV nm (log ε): 280 (3.85), 210 (4.24); ^1H NMR ($CDCl_3$): δ 0.61 (3H, *d*, *J* = 7.0 Hz, 3-Me), 1.00 (3H, *d*, *J* = 6.4 Hz, 4-Me), 2.44 (2H, *m*, H-3,4), 3.88 (3H, *s*, OMe), 3.91 (3H, *s*, OMe), 4.64 (1H, *d*, *J* = 9.2 Hz, H-5), 5.45 (1H, *d*, *J* = 4.4 Hz, H-2), 5.52 (1H, *br*, OH), 5.56 (1H, *br*, OH), 6.79–6.95 (6H, *m*, Ar-H); MS (*m/z*): 344 $[M]^+$, 271, 192, 145, 124.

Table 1. ^{13}C NMR chemical shifts (δ) of compounds **1–6** 100 MHz $CDCl_3$

	1	**2**	**3**	**4**	**5**	**6**
1′	134.0	134.7	134.2	134.8	133.1	132.7
2′	107.9	108.0	109.2	109.8	103.2	108.8
3′	146.5	149.0	146.5	148.9	146.9	146.7
4′	145.1	148.5	145.0	148.3	134.0	144.4
5′	114.1	111.1	114.1	111.1	146.9	114.4
6′	119.9	118.6	119.3	118.5	103.2	118.9
2	87.3[a]	87.4	87.3	87.2[a]	87.2[a]	84.8
3	44.4[b]	44.5	44.3	44.2[b]	44.5[b]	47.6
4	44.5[b]	44.5	44.3	44.3[b]	44.0[b]	43.5
5	87.4[a]	87.4	87.3	87.3[a]	87.5[a]	85.8
1″	136.2	136.2	134.2	134.1	134.0	135.1
2″	106.8	106.8	109.2	109.1	109.0	108.4
3″	147.7	147.8	146.5	146.5	146.5	146.3
4″	146.9	147.0	145.0	145.0	145.0	145.1
5″	109.0	109.8	114.1	114.1	114.0	114.1
6″	119.3	119.9	119.3	119.2	120.0	119.3
3-Me	12.8	12.8[a]	12.9	12.8[c]	13.2	9.4
4-Me	12.8	12.9[a]	12.9	12.9[c]	12.8	11.9
OMe	55.9	56.0	55.8	55.7	55.9	56.0
OMe		55.9	55.8	55.9	56.3	56.0
OMe				55.7	56.3	
OCH_2O	100.9	100.9				

[a, b, c] Assignments are interchangable.

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CLEOMISCOSIN D, A COUMARINO-LIGNAN FROM SEEDS OF *CLEOME VISCOSA*

SANDEEP KUMAR, ANIL B. RAY, CHOHACHI KONNO,* YOSHITERU OSHIMA* and HIROSHI HIKINO*

Department of Medicinal Chemistry, I. M. S., Banaras Hindu University, Varanasi 221005, India; * Pharmaceutical Institute, Tohoku University, Aoba-Yama, Sendai 980, Japan

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Key Word Index—*Cleome viscosa*; Capparidaceae; cleomiscosin D; coumarino-lignan.

Abstract—Cleomiscosin D, a minor coumarino-lignan of the seeds of *Cleome viscosa*, has been proved to be regioisomer of cleomiscosin C. A method of degradation of coumarino-lignans for the identification of the coumarin moiety has been developed.

INTRODUCTION

Cleomiscosins A (**1**) and B (**2**), isolated from the seeds of *Cleome viscosa* Linné and fully characterized from comprehensive spectral analysis and some chemical reactions, constitute the first regioisomeric pair of coumarino-lignans in which a coumarin moiety is linked with a phenylpropanoid unit through a dioxane bridge [1–3]. The correctness of these structures were later verified by Merlini and co-workers who achieved their synthesis by oxidative coupling of fraxetin with coniferyl alcohol [4]. We subsequently reported the isolation of a third coumarino-lignan, cleomiscosin C (**3**) from this source [3] and showed it to be identical with aquillochin [5] for which two alternative structures were proposed. Further investigation on this plant material led us to isolate a known coumarin and a new coumarinolignan, cleomiscosin D. The characterization of these two compounds and a method of cleaving the dioxane bridge of cleomiscosins for identification of coumarin moieties will be discussed in the present paper.

RESULTS AND DISCUSSION

A coumarin, $C_{10}H_8O_5$ (MS *m/z* 208, M^+), was recognized to be oxygenated at its 6, 7 and 8-positions from its UV, IR spectra together with its ^1H NMR signals for two coumarin hydrogens [δ6.17 and 7.74 (1H each, *d*, $J = 9.5$ Hz)], a lone aromatic hydrogen (δ6.61) and a methoxyl grouping (δ3.88). Irradiation of the methoxyl signal at δ3.88 showed an observable NOE of the isolated signal at δ6.61 which in turn showed long range coupling with the coumarin H-4 signal at δ7.74. The observation clearly revealed it to be fraxetin [4].

Cleomiscosin D (**4**), $C_{21}H_{20}O_9$ (MS, *m/z* 416, M^+), responded to tests for phenol. The UV and IR data of cleomiscosin D were essentially identical with those of cleomiscosin C (**3**), an isomer of cleomiscosin D. The ^{13}C NMR spectrum of cleomiscosin D disclosed the presence of eight aliphatic carbons (Me–O × 3, $-CH_2-O$ × 1, > CH–O × 2, –CH=CH– × 1), 12 aromatic carbons (CH × 3, C × 2, C–O × 7) and one carbonyl-like cleomiscosin C. Cleomiscosin D gave a diacetate (**4a**), $C_{25}H_{24}O_{11}$ (MS, *m/z* 500, M^+).

The ^1H NMR spectrum of cleomiscosin D in pyridine-d_5 showed signals for three methoxyl groupings (δ3.77, 3.77 and 3.82), two coumarin hydrogens (δ6.41 and 7.73), an isolated aromatic hydrogen (δ6.74) and four aliphatic hydrogens on carbons carrying oxygen functions (δ3.96, 4.30, 4.57 and 5.55). Significant amounts of NOE were observed between the isolated signal at δ6.74 and a methoxyl signal at 3.82, between the isolated signal at 6.74