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LIGNANS FROM *MACHILUS THUNBERGII*

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Key Word Index—*Machilus thunbergii*; Lauraceae; bark; 1,4-diaryl-2,3-dimethylbutane lignans; benzofuran neolignans; β-aryloxyarylpropane neolignans; machilin A, B, C, D, E.

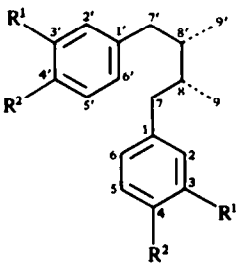
Abstract—Five new lignans, machilin A [(2*S*,3*R*)-2,3-dimethyl-1,4-dipiperonyl-butane], machilin B [(2*S*,3*S*)-2,3-dihydro-7-methoxy-3-methyl-2-piperonyl-5-*trans*-(3-hydroxy-1-propenyl)benzofuran], machilin C, D [*erythro*- and *threo*-2-(2-methoxy-4-*trans*-propenylphenoxy)-1-(4-hydroxy-3-methoxyphenyl)propan-1-ol], machilin E (*erythro*-1-acetoxy-2-[2-methoxy-4-*trans*-(3-hydroxy-1-propenyl)phenoxy]-1-piperonylpropane) were isolated from the bark of *Machilus thunbergii* and their structures were characterized.

INTRODUCTION

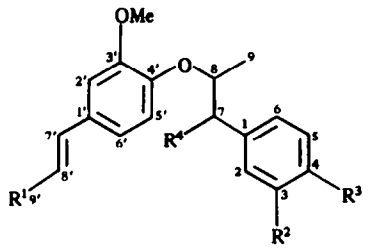
The bark and root of *Machilus thunbergii* Sieb. et Zucc. have been used as in traditional Chinese medicine [1]. Several alkaloids have been isolated from the root [2]. However, no study of the chemical constituents of the bark has been carried out. In this paper, we report five new lignans, machilin A, B, C, D and E in addition to the known compounds, meso-dihydroguaiaretic acid [3] and licarin A and B [4].

RESULTS AND DISCUSSION

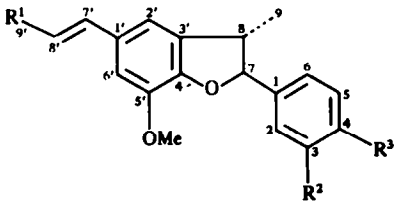
The bark of *Machilus thunbergii* was extracted with MeOH. From the $CHCl_3$-soluble portion of the MeOH extract, compounds **1**–**8** were obtained by column chromatography. Machilin A (**1**), $C_{22}H_{22}O_4$, was obtained as colourless needles. The IR, EI-MS, ^1H NMR and ^{13}C NMR spectral data of **1** indicated the planar structure of **1** was the same as that of austrobailignan 5 [5]. Compound **1**, however, showed no optical activity. In



	R^1	R^2
1	OCH_2O	
6	OMe	OH



	R^1	R^2	R^3	R^4	
3	Me	OMe	OH	OH	(*erythro*)
4	Me	OMe	OH	OH	(*threo*)
5	CH_2OH	OCH_2O		OAc	(*erythro*)



	R^1	R^2	R^3
2	CH_2OH	OCH_2O	
7	Me	OMe	OH
8	Me	OCH_2O	

order to elucidate the absolute configuration, **1** was halogenated with phosphorus pentachloride, and hydrolysed into the catechol (**1a**) [6], which was identified as nordihydroguaiaretic acid by direct GC comparison and mixed melting point with an authentic sample. Thus, **1** has the 2*S* and 3*R* configuration (*meso*-form).

Machilin B (**2**), $C_{20}H_{20}O_5$, was obtained as colourless oil. The presence of a hydroxyl group was indicated by the peak at 3500 cm^{-1} in the IR spectrum. The ^1H NMR spectrum of **2** was similar to that of licarin B, belonging to the benzofuran type of neolignan, except for the signals of a propenyl group of **2** which appeared at δ 6.56 (H-7′), δ 6.23 (H-8′) and δ 4.30 (H-9′). The signals of the methylene group (δ 4.71, 2H, *m*) due to H-9′ in the monoacetate **2a** were shifted further downfield than those of **2** in the ^1H NMR spectrum. These data indicated that the hydroxyl group is attached to the C-9′ position. Thus, **2** is 2,3-dihydro-7-methoxy-3-methyl-2-piperonyl-5-*trans*-(3-hydroxy-1-propenyl)benzofuran. The relative configuration of **2** was deduced from the chemical shift of H-7 (δ 5.11) and H-9 (δ 1.38) [7]. The absolute configuration of **2** was determined as 2*S* and 3*S* by comparing the specific rotation of **2** ($[\alpha]_D^{25}$ −40.1) with the previously reported licarin B ($[\alpha]_D^{25}$ −44.0).

Machilin C (**3**), $C_{20}H_{24}O_5$, was obtained as colourless oil. In the IR spectrum, the presence of hydroxyl group(s) was indicated by the peak at 3500 cm^{-1}. On acetylation, **3** afforded a diacetate (**3a**), the ^1H NMR spectrum of which showed a change in the chemical shift of one proton from δ 4.82 to δ 5.93 indicating the presence of a hydroxyl group bearing the methine carbon. Furthermore, a decoupling experiment indicated the presence of a CH_3–CH–CH(OH)– group. The above results and ^1H NMR spectral data placed **3** in the group of β-aryloxyarylpropane type neolignans [8], and the structure of **3** was determined as 2-(2-methoxy-4-*trans*-propenylphenoxy)-1-(4-hydroxy-3-methoxyphenyl) propan-1-ol by the ^{13}C NMR spectrum. Comparison of the values of the chemical shift and the coupling constant of H-7 and H-8 with reported values indicated that **3** belongs to the *erythro* series [9].

Machilin D (**4**), $C_{20}H_{24}O_5$, was obtained as colourless oil. By the IR, EI-MS, ^1H NMR and ^{13}C NMR spectra, the planar structure of **4** was the same as that of **3**. However, the coupling constant and chemical shift of H-7 and H-8 and the value of the specific rotation of **4** differed from those of **3**. Thus, **4** is the *threo*-diasteroisomer of **3** [9].

Machilin E (**5**), $C_{22}H_{24}O_7$, was obtained as yellowish oil. The EI-MS showed a molecular ion peak at *m/z* 400. The ^1H NMR spectral data suggested that the structure of **5** was close to that of **3**. The ^1H NMR spectrum also showed the presence of an acetoxyl group, a methylenedioxyl group and a –CH=CH–CH_2OH group. The value of the chemical shift of H-7 (δ 5.83) of **5** was similar to that of **3a** (δ 5.93), which indicated that the acetoxyl group is attached to the C-7 hydroxyl. Thus, **5** is 1-acetoxy- 2-[2-methoxy- 4-*trans*- (3-hydroxy-1-propenyl) phenoxy]- 1-piperonylpropane. The small coupling constant of H-7 (J = 4.1) indicated that **5** belongs to the *erythro* series.

Machilin A–E have not been reported as naturally occurring lignans. Compounds **6** (1.3 mg), **7** (25.5 mg) and **8** (0.79 mg) were identified as *meso*-dihydroguiaretic acid, licarin A and B, respectively, by comparison of their spectral data with the reported data [3, 4]. Compounds **6–8** have never been isolated from this plant before.

EXPERIMENTAL

The NMR spectra were measured at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR. The chemical shifts were given on the δ (ppm) scale with TMS as internal standard.

Table 1. ^{13}C NMR chemical shifts (δ) of lignans **1–5** 100 MHz $CDCl_3$

	1		2	3	4	5
1,1′	135.6	1	134.2	133.7	132.0	131.6
2,2′	108.0	2	106.7	108.9	109.3	107.9
3,3′	145.5	3	147.5	146.5	146.6	148.0
4,4′	147.5	4	147.2	144.8	145.5	148.5
5,5′	109.3	5	108.1	113.9	114.1	110.3
6,6′	121.7	6	120.2	119.9	120.8	119.5
7,7′	39.4	7	93.5	82.4	84.2	93.8
8,8′	39.0	8	45.7	73.6	78.5	78.2
9,9′	16.1	9	18.0	13.4	17.1	15.4
OCH_2O	100.7	1′	131.5	131.9	130.5	130.1
		2′	114.3	109.4	109.4	108.6
		3′	133.3	145.6	146.8	147.1
		4′	146.0	151.5	150.8	151.1
		5′	143.7	119.1	118.8	118.0
		6′	110.1	119.0	119.1	121.1
		7′	130.8	130.5	130.5	131.1
		8′	126.2	125.0	124.9	127.1
		9′	63.8	18.3	18.4	63.8
		OCH_3	56.0	56.0	56.0	55.9
		OCH_3		56.0	56.0	
		OCH_2O	101.1			101.1
		AcC=O				170.1
		AcMe				21.1

Isolation. The air-dried bark of *Machilus thunbergii* (5 kg) collected at Izu Peninsula in April, 1985, were extracted with hot MeOH. The concd extract was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was chromatographed on silica gel with the *n*-hexane–EtOAc system.

Machilin A (**1**). Colourless needles. 1.7 g. mp 48–50°. $[\alpha]_D^{25}$ 0° ($CHCl_3$, *c* = 0.4). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2900, 1605, 1503, 1495, 1450; ^1H NMR δ ($CDCl_3$): 0.86 (6H, *d*, *J* = 6.7 Hz, H-9,9'), 1.76 (2H, *m*, H-8,8'), 2.29 (2H, *dd*, *J* = 13.4, 9.3 Hz, H-7a,7'a), 2.74 (2H, *dd*, *J* = 13.4, 4.8 Hz, H-7b, 7'b), 5.90 (4H, *s*, OCH_2O × 2), 6.51 (2H, *dd*, *J* = 7.8, 1.6 Hz, H-6,6'), 6.67 (2H, *d*, *J* = 1.6 Hz, H-2,2'), 6.76 (2H, *d*, *J* = 7.8 Hz, H-5,5'); MS (*m/z*): 326 $[M]^+$, 137, 77.

Cleavage of the methylenedioxyl group of **1**. Compound **1** (100 mg) was dissolved in dried CH_2Cl_2, the solution was refluxed in the presence of PCl_5 (84.4 mg) at 60–70° for 3 hr, then a small amount of H_2O was added to the reaction mixture and the mixture was refluxed for 3 hr. The product was chromatographed on silica gel with $CHCl_3$–Me_2CO (3 : 1). **1a** was obtained from the most polar fraction. **1a**: tan crystals. mp 173° (*n*-hexane, Me_2CO). ^1H NMR δ (acetone-d_6): 0.81 (6H, *d*, *J* = 6.7 Hz, H-9,9'), 1.73 (2H, *m*, H-8,8'), 2.20 (2H, *dd*, *J* = 13.4, 9.4 Hz, H-7a,7'a), 2.68 (2H, *dd*, *J* = 13.4, 4.8 Hz, H-7b,7'b), 6.51 (2H, *dd*, *J* = 7.8, 1.6 Hz, H-6,6'), 6.68 (2H, *d*, *J* = 1.6 Hz, H-2,2'), 6.72 (2H, *d*, *J* = 7.8 Hz, H-5,5'); MS (*m/z*): 302 $[M]^+$, 123, 77.

Machilin B (**2**). Colourless oil. 22.3 mg. $[\alpha]_D^{25}$ −40.1 ($CHCl_3$, *c* = 0.11). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 2950, 1610, 1500, 1450, ^1H NMR δ ($CDCl_3$): 1.38 (3H, *d*, *J* = 6.8 Hz, H-9), 3.41 (1H, *m*, H-8), 3.89 (3H, *s*, OCH_3), 4.30 (2H, *m*, H-9'), 5.11 (1H, *d*, *J* = 8.9 Hz, H-7), 5.94 (2H, *s*, OCH_2O), 6.23 (1H, *dt*, *J* = 15.8, 6.0 Hz, H-8'), 6.56 (1H, *m*, H-7'), 6.80–6.90 (5H, *m*, Ar–H); MS (*m/z*): 340 $[M]^+$, 259, 175, 135, 77. On acetylation with pyridine and Ac_2CO, **2** afforded a monoacetate (**2a**): IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 1730, 1610, 1500, 1450; ^1H NMR δ($CDCl_3$): 1.38 (3H, *d*, *J* = 6.8 Hz, H-9), 2.10 (3H, *s*, $OCOCH_3$), 3.42 (1H, *m*, H-8), 3.89(3H, *s*, OCH_3), 4.71 (2H, *m*, H-9'), 5.12 (1H, *d*, *J* = 8.9 Hz, H-7), 5.95 (2H, *s*, OCH_2O), 6.16 (1H, *dt*, *J* = 15.7, 6.0 Hz, H-8'), 6.60 (1H, *m*, H-7'), 6.80–6.90 (5H, *m*, Ar–H); MS (*m/z*): 382 $[M]^+$, 327, 182, 135.

Machilin C (**3**). Colourless oil. 10.6 mg. $[\alpha]_D^{25}$ −16.5° ($CHCl_3$, *c* = 0.27). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2950, 1610, 1520; ^1HNMR δ ($CDCl_3$); 1.17 (3H, *d*, *J* = 6.4 Hz, H-9), 1.88 (3H, *dd*, *J* = 6.6, 1.6 Hz, H-9'), 3.88 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 4.33 (1H, *m*, H-8), 4.82 (1H, *d*, *J* = 2.9 Hz, H-7), 5.60 (1H, *br*, OH), 6.15 (1H, *dq*, *J* = 15.6, 6.6 Hz, H-8'), 6.36 (1H, *m*, H-7'), 6.75–7.00 (6H, *m*, Ar–H); MS (*m/z*): 344 $[M]^+$, 192, 164, 137. Diacetate (**3a**): IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2950, 1740, 1600, 1505; ^1H NMR δ($CDCl_3$): 1.30 (3H, *d*, *J* = 6.4 Hz, H-9), 1.86 (3H, *dd*, *J* = 6.6, 1.7 Hz, H-9'), 2.12 (3H, *s*, $OCOCH_3$), 2.31 (3H, *s*, $OCOCH_3$), 3.80 (3H, *s*, OCH_3), 3.83 (3H, *s*, OCH_3), 4.53 (1H, *m*, H-8), 5.93 (1H, *d*, *J* = 4.2 Hz, H-7), 6.11 (1H, *dq*, *J* = 15.7, 6.6 Hz, H-8'), 6.32 (1H, *m*, H-7'), 6.8–7.1 (6H, *m*, Ar–H); MS (*m/z*): 428 $[M]^+$, 265, 223, 164, 91.

Machilin D (**4**). Colourless oil. 3.5 mg. $[\alpha]_D^{25}$ 38.1° ($CHCl_3$, *c* = 0.07). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2900, 1590, 1490. ^1H NMR δ ($CDCl_3$): 1.16 (3H, *d*, *J* = 6.2 Hz, H-9), 1.87 (3H, *dd*, J = 6.6, 1.6 Hz, H-9'), 3.90 (3H, *s*, OCH_3), 3.91 (3H, *s*, OCH_3), 4.08 (1H, *m*, H-8), 4.61 (1H, *d*, *J* = 8.4 Hz, H-7), 5.60 (1H, *br*, OH), 6.14 (1H, *dt*, *J* = 15.6, 6.5 Hz, H-8'), 6.35 (1H, *m*, H-7'), 6.85–6.95 (6H, *m*, Ar–H); MS (*m/z*): 344 $[M]^+$, 191, 164, 91, 57.

Machilin E (**5**). Yellowish oil. 5.6 mg. $[\alpha]_D^{25}$ 29.2° ($CHCl_3$, *c* = 0.11) IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 2950, 1730, 1600, 1505, ^1H NMR δ ($CDCl_3$): 1.29 (3H, *d*, *J* = 6.6 Hz, H-9), 2.09 (3H, *s*, $OCOCH_3$), 3.83 (3H, *s*, OCH_3), 4.30 (2H, *m*, H-9'), 4.54 (1H,*m*, H-8), 5.83 (1H, *d*, *J* = 4.1 Hz, H-7), 5.90 (2H, *s*, OCH_2O), 6.25 (1H, *dt*, *J* = 15.8, 6.0 Hz, H-8'), 6.54 (1H, *m*, H-7'), 6.82–6.98 (5H, *m*, Ar–H); MS (*m/z*): 400 $[M]^+$, 356, 329, 221, 180, 151, 91.

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REFERENCES

1. Jiang-su-xin-yi-xue-yuan (1978) *Zhong-yao-da-ci-dian Vol* **1**, 1009.
2. Tomita, M. and Kozuka, M. (1963) *Yakugaku Zasshi* **84**, 362.
3. Ikeya, Y., Taguchi, I. and Yoshida, I. (1979) *Chem. Pharm. Bull.* **27**, 1583.
4. Aiba, C. J., Correa, R. G. C. and Gottlieb, O. R. (1973) *Phytochemistry* **12**, 1163.
5. Murphy, S. T., Ritchie, E. and Taylor, W. C. (1975) *Aust. J. Chem.* **28**, 81.
6. Trammel, G. L. (1978) *Tetrahedron Letters* **18**, 1525.
7. Aiba, C. J., Frenandes, J. B., Gottlieb, O. R. and Maia, J. G. S. (1975) *Phytochemistry* **14**, 1597.
8. Barata, L. E. S., Baker, P. M., Gottlieb, O. R. and Ruveda, E. A. (1978) *Phytochemistry* **17**, 783.
9. Sarkanen, K. V. and Wallis, A. F. A. (1973) *J. Chem. Soc. Perkin Trans. I* 1869.