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TWO FLAVONOIDS FROM TWO *LINDERA UMBELLATA* VARIETIES

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Key Word Index—*Lindera umbellata* var. *membranacea*; *L. umbellata* var. *lancea*; Lauraceae; chalcone; dihydrochalcone; linderachalcone; methyllinderatin; *p*-menthene.

Abstract—A new chalcone, linderachalcone, and a new dihydrochalcone, methyllinderatin, were isolated from the leaves of *Lindera umbellata* var. *membranacea* and *L. umbellata* var. *lancea*, respectively. Their structures were established by spectroscopic and chemical means.

INTRODUCTION

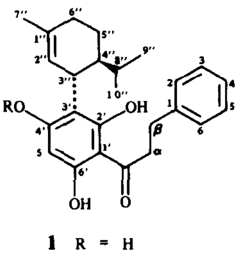
Previously, we have reported the isolation and the structural determination of a series of novel *p*-menthene substituted flavonoids; linderatin (**1**), linderatone (**2**), methyllinderatone (**3**), and isolinderatone (**4**), from *Lindera umbellata* Thunb. var. *lancea* Momiyama, *L. umbellata* Thunb. and *L. umbellata* Thunb. var. *membranacea* (Maxim.) Momiyama [1–4]. In the course of our further examination of the leaves of these plants, we isolated a new chalcone, linderachalcone (**5**), from *L. umbellata* var. *membranacea* and a new dihydrochalcone, methyllinderatin (**6**), from *L. umbellata* var. *lancea*. We now describe the isolation and characterization of these new compounds (**5** and **6**).

RESULTS AND DISCUSSION

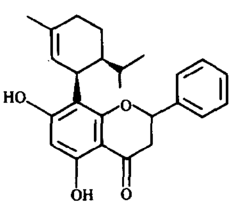
Linderachalcone (**5**), $C_{25}H_{28}O_4$ gave a brown colour with ethanolic ferric chloride and the IR spectrum showed absorption bands for hydroxyl (3575 and 3350 cm^{-1}) and conjugated carbonyl (1625 cm^{-1}) groups. In the ^{1}H NMR spectrum, signals of three methyl groups (δ 0.84 and 0.86, 6H, *d* × 2, $J = 7.1$ Hz; δ 1.67, 3H, *s*), a benzylic methine proton (δ 3.89, 1H, *d*, $J = 10.4$ Hz), an olefinic proton (δ 5.26, 1H, *s*), an aromatic proton (δ 6.06, 1H, *s*), a phenyl group (δ 7.43, 3H, *m*; δ 7.71, 2H, *m*), a *trans* olefinic group (δ 7.78, 1H, *d*, $J = 15.8$ Hz; δ 8.25, 1H, *d*, $J = 15.8$ Hz), and two hydroxyl groups (δ 8.65 and 10.00, 2H, *br s* × 2) were observed. In the ^{13}C NMR spectra (Table 1), all the chemical shifts of the signals of **5** were very similar to those of linderatin (**1**) [1] except for the signals of C=O (δ 193.1), C-α (δ 130.1), and C-β (δ 142.7). The mass spectrum of **5** showed a molecular ion peak at m/z 392 which indicates a decrease of two mass units in comparison with that of **1**. This spectrum also had a characteristic fragmentation peak at m/z 322 $[M-70]^+$ which was formed by the retro-Diels–Alder reaction [1] of a *p*-menthene unit as in **1**. These results suggested that the structure of linderachalcone would be represented by the formula **5**.

In order to confirm the structure of **5** the following study was also carried out. Hydrogenation of **5** with Pd-C in methanol gave linderatin (**1**) as a predominant product. On the other hand, **5** was derived by treatment of linderatone (**2**) [2] with potassium hydroxide in methanol. Therefore, the structure of linderachalcone is established as **5**. This is the first chalcone with a *p*-menthene substituent to be reported in nature.

Methyllinderatin (**6**), $C_{26}H_{32}O_4$ gave a brown colour with ethanolic ferric chloride and the IR spectrum showed absorption bands for hydroxyl (3360 cm^{-1}) and conjugated carbonyl (1630 cm^{-1}) groups. In the ^{1}H NMR spectrum, signals of three methyl groups (δ 0.81 and 0.84, 6H, *d* × 2, $J = 7.4$ Hz; δ 1.79, 3H, *s*), an ethylene group (δ 3.00, 2H, *t*, $J = 7.4$ Hz; δ 3.39, 2H, *t*, $J = 7.4$ Hz), a methoxyl group (δ 3.79, 3H, *s*), a benzylic methine proton (δ 3.87, 1H, *br d*, $J = 10.4$ Hz), an olefinic proton (δ 5.46, 1H, *s*), an aromatic proton (δ 6.05, 1H, *s*), a hydroxyl group (δ 7.05, 1H, *s*), a phenyl group (δ 7.27, 5H, *br s*), and a chelated hydroxyl group (δ 13.71, 1H, *s*) were observed. In the ^{13}C NMR spectra (Table 1), all the chemical shifts of the signals of **6** were very similar to those of linderatin (**1**) except for the signal of C-5′ (δ 91.7) and the presence of a methoxyl group (δ 55.8). The mass spectrum of **6** showed



1 R = H
6 R = Me



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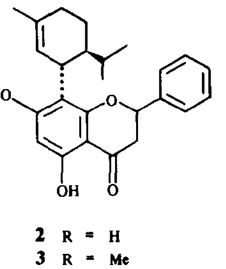
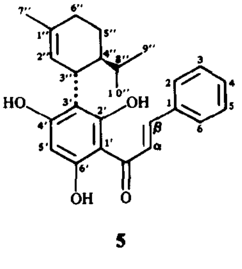


2 R = H
3 R = Me



5

a molecular ion peak at *m/z* 408 which indicates an increase of 14 mass units in comparison with **1**. This spectrum also had a characteristic fragmentation peak at *m/z* 338 $[M-70]^+$ which was formed by the retro-Diels–Alder reaction [1] of a *p*-menthene unit as in **1**. These results suggested that **6** would be a monomethyl derivative of **1**.

The structure of methyllinderatin was confirmed as follows. Hydrogenolysis of methyllinderatone (**3**) [3] with Raney Ni in ethanol afforded a 4′-methoxydihydrochalcone (**6**), which was identical with methyllinderatin. Thus, the structure of methyllinderatin is represented by the formula **6**.

EXPERIMENTAL

Mps were uncorr. CC was run on Florisil (100–200 mesh) and Merck silica gel 60 (70–230 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 with TMS as int. standard. Chemical shifts are in ppm.

Extraction and separation of compounds. The MeOH extract of the fresh leaves (6.0 kg) of *Lindera umbellata* var. *membranacea* collected in Gifu prefecture in July 1985 was divided into *n*-hexane (86 g) and $CHCl_3$ (290 g) soluble fractions. A portion of the *n*-hexane soluble fraction (8.2 g) was chromatographed on a column of florisil (*n*-hexane–Et_2O, 5:1) and subsequently repeated prep. TLC afforded linderachalcone (**5**, 35 mg).

Table 1. ^{13}C NMR spectral data (25.0 MHz, acetone-d_6) of **1**, **5**, and **6**

C	**1**	**5**	**6**
1	143.2	140.9	142.8
2	129.4	128.8	129.1
3	129.6	128.5	129.2
4	127.1	127.7	126.7
5	129.6	128.5	129.2
6	129.4	128.8	129.1
1′	105.4	106.0	105.5
2′	161.4*	159.2*	162.1*
3′	110.5	109.5	111.5
4′	163.9*	162.2*	163.7*
5′	95.8	96.1	91.7
6′	165.9*	164.3*	165.2*
C=O	205.9	193.1	205.7
C=α	46.6	130.1	46.7
C=β	31.5	142.7	31.4
OMe	–	–	55.8
1″	135.4	135.6	133.9
2″	126.9	124.7	126.5
3″	36.0†	34.9†	35.9†
4″	43.0	44.0	42.6
5″	23.7	22.2	23.6
6″	31.5	30.7	31.4
7″	23.7	23.8	23.6
8″	29.1†	27.9†	29.1†
9″	16.9	16.6	16.7
10″	22.0	21.8	21.9

*, † Assignments may be interchanged.

The extraction and fractionation of the leaves of *Lindera umbellata* var. *lancea* have been previously described [4]. A portion of the *n*-hexane soluble fraction (3.0 g) was chromatographed on a column of florisil (*n*-hexane–EtOAc, 5:1) and subsequently repeated prep. TLC afforded methyllinderatin (**6**, 30 mg).

Linderachalcone (**5**). Yellow oil. $[\alpha]_D$ +17.8° ($CHCl_3$, *c* 0.40). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3575, 3350, 1625, 1600. UV λ_{max}^{EtOH} nm: 218 (sh), 310 (sh), 347. MS *m/z*: 392 (M^+), 322, 307. HRMS *m/z*: 392.1960 (M^+, calcd for $C_{25}H_{28}O_4$: 392.1986); 322.1177 ($[M-70]^+$, calcd for $C_{20}H_{18}O_4$: 322.1203). ^{1}H NMR (Me_2CO-d_6): δ0.84, 0.86 (6H, *d* × 2, $J=7.1$ Hz, 2 × 8″-Me), 1.67 (3H, *s*, 1″-Me), 3.89 (1H, *d*, $J=10.4$ Hz, 3″-H), 5.26 (1H, *s*, 2″-H), 6.06 (1H, *s*, 5′-H), 7.43 (3H, *m*, Ar–H), 7.71 (2H, *m*, Ar–H), 7.78 (1H, *d*, $J=15.8$ Hz, β-H), 8.25 (1H, *d*, $J=15.8$ Hz, α-H), 8.65 (1H, *br s*, OH), 10.00 (1H, *br s*, OH).

Methyllinderatin (**6**). Colourless oil. $[\alpha]_D$ +41.0° ($CHCl_3$, *c* 0.40). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360, 1630, 1590. UV λ_{max}^{EtOH} nm: 225 (sh), 288. MS *m/z*: 408 (M^+), 338, 323. HRMS *m/z*: 408.2306 (M^+, calcd for $C_{26}H_{32}O_4$: 408.2299), 338.1546 ($[M-70]^+$, calcd for $C_{21}H_{22}O_4$: 338.1517). ^{1}H NMR ($CDCl_3$): δ0.81, 0.84 (6H, *d* × 2, $J=7.4$ Hz, 2 × 8″-Me), 1.79 (3H, *s*, 1″-Me), 3.00 (2H, *t*, $J=7.4$ Hz, β-H), 3.39 (2H, *t*, $J=7.4$ Hz, α-H), 3.79 (3H, *s*, OMe), 3.87 (1H, *br d*, $J=10.4$ Hz, 3″-H), 5.46 (1H, *s*, 2″-H), 6.05 (1H, *s*, 5′-H), 7.05 (1H, *s*, 2′-OH), 7.27 (5H, *br s*, Ar–H), 13.71 (1H, *s*, OH).

Hydrogenation of linderachalcone. A suspension of **5** (4 mg) and 10% Pd-C (4 mg) in MeOH (1 ml) were stirred under H_2 for 20 min. The reaction mixture was filtered and the filtrate evapd to dryness. The residue was purified by prep. TLC ($CHCl_3$–Me_2CO, 10:1) to give a colourless oil (2 mg). This compound was identical with linderatin (**1**).

Cleavage of linderatone. A mixture of linderatone (**2**, 40 mg) and KOH (500 mg) in MeOH (3 ml) was refluxed for 10 min. After cooling, a small amount of ice was added, the mixture neutralized with dil. HCl and then extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried over Na_2SO_4, and evapd to dryness. The residue was purified by prep. TLC ($CHCl_3$–Me_2CO, 10:1) to afford a yellow oil (7 mg) which was identical with linderachalcone (**5**).

Hydrogenolysis of methyllinderatone. A suspension of methyllinderatone (**3**, 10 mg) and Raney Ni (W-3) in EtOH (1 ml) was stirred under H_2 for 20 min. The reaction mixture was filtered and the filtrate evapd to dryness. The residue was purified by prep. TLC (*n*-hexane–Et_2O, 3:1) to afford a colourless oil (2 mg) which was identical with methyllinderatin (**6**).

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