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A CHALCONE DERIVATIVE FROM THE BARK OF *LINDERA UMBELLATA*

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Key Word Index—*Lindera umbellata*; Lauraceae; bark; flavonoid; chalcone; monoterpenoid; *p*-menthene.

Abstract—The bark of *Lindera umbellata* has yielded a novel chalcone derivative, 2′,6′-dihydroxy-4′-methoxy-3′-(3″-methyl-6″-methylethyl-2″-cyclohexenyl)chalcone, in addition to several known compounds. Their structures have been determined by spectroscopic method.

INTRODUCTION

Lauraceous plants have widespread use in both oriental medicine and occidental medicine. Our previous studies on the chemical constituents of these plants have led to the isolation and structural elucidation of new neolignans, machilin A–E and tetrahydrofuran lignans, from the bark of *Machilus thunbergii* [1, 2], and thalictoside and its phenylpropanoid ester both of which have an aliphatic nitro group from the bark of *Parabenzoin praecox* [3].

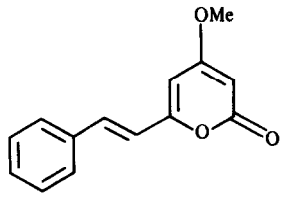
Lindera umbellata Thunb. is a deciduous shrub distributed in the mountainous region of Japan. The roots, root bark and xylem have been used as a crude drug in traditional Chinese medicine [4], and several phytochemical investigations have so far been carried out [5–15]. This paper refers to the isolation and characterization of a new chalcone derivative in addition to several known compounds from the methanolic extract of *L. umbellata*.

RESULTS AND DISCUSSION

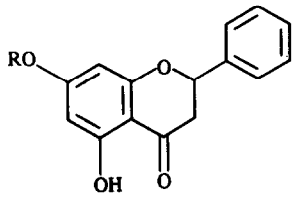
The bark of *L. umbellata* was extracted with hot methanol. Chromatography on a silica gel column of the chloroform-soluble portion of the methanol extract gave compounds **1**–**5**.

Compounds **1**–**4** were identified as 5,6-dehydrokawain [16, 17], (±)-pinostrobin [18, 19], (±)-pinocembrin [20, 21] and 2′,6′-dihydroxy-4′-methoxychalcone [8] by comparison of their spectral data and physical properties with literature values.

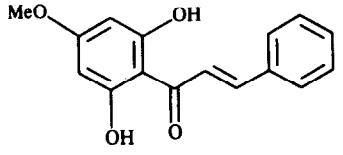
Compound **5** was a yellow powder with a molecular formula $C_{26}H_{30}O_4$ (HRMS). It gave a positive colour with benzidine reagent. The UV spectrum of **5** had absorptions at 214 (log ε 4.49), 308 shoulder (4.25) and 343 nm (4.44). The IR spectrum was consistent with the presence of hydroxyl group(s) (3350 cm^{-1}), and a carbonyl group (1620 cm^{-1}) conjugated with an alkene and an aromatic ring whose absorption at lower wavenumbers than expected (1665 cm^{-1}) seemed to be due to the formation of an intramolecular hydrogen bond. Acetylation of **5** with acetic anhydride in pyridine gave the corresponding diacetate (**5a**) as a pale-yellow amorphous powder. The EIMS of **5a** exhibited a molecular ion peak at *m/z* 490. The ^{13}C NMR data (Table 1) were of particular help in elucidating the structure of **5**. Compound **5** had the same chalcone skeleton as **4**, and a $C_{10}H_{17}$ unit for the remaining structure. The presence of the chalcone skeleton was also supported by the ^1H NMR data [aromatic protons of chalcone A ring: δ7.63 (2H, *dd*, *J* = 7.8, 2.0 Hz) and 7.44–7.35 (3H); *trans* alkene protons: δ8.01 and 7.80 (each 1H, *d*, *J* = 15.6 Hz); an aromatic proton of chalcone B ring: δ6.09 (1H, *s*); methoxyl protons: δ3.81 (3H, *s*); two hydroxyl protons: δ14.04 and 7.15 (each 1H, *br s*, disappeared on addition of CD_3OD)] and EIMS (a



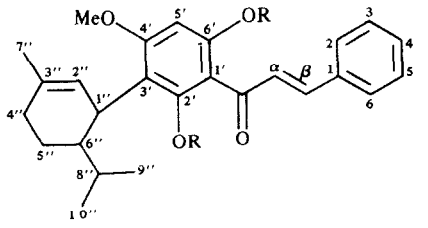
1



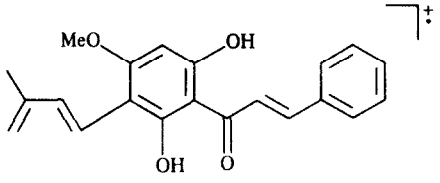
	R
2	Me
3	H



4



	R
5	H
5a	Ac



5b

Table 1. ^{13}C NMR spectral data for **4** and **5** (100.6 MHz, acetone-d_6, TMS as int. standard)

C	4	5
Chalcone moiety		
1	136.5	136.5
2	129.1	129.1
3	129.8	129.7
4	130.9	130.8
5	129.8	129.7
6	129.1	129.1
α	128.4	128.8
β	142.9	142.6
C=O	193.4	193.8
1′	106.2	106.3
2′	165.4	165.6[a]
3′	94.6	111.8
4′	167.2	164.3[a]
5′	94.6	92.1
6′	165.4	162.1[a]
OMe	55.8	55.9
p-Menthene moiety		
1″		36.0
2″		126.7
3″		129.7
4″		31.5
5″		23.8
6″		42.7
7″		23.6
8″		29.2
9″		16.7[b]
10″		21.9[b]

[a, b] Assignments may be reversed.

fragment ion peak at *m/z* 270). The $C_{10}H_{17}$ substituent was concluded to be a *p*-menthene group at the ring junction to chalcone C-3′ on the basis of the ^{1}H NMR and ^{1}H–^{1}H COSY spectra, in which a methyl group on a double bond, an olefinic proton, an isopropyl group and an aromatic proton arising from chalcone B ring (H-5′) were present. Furthermore, the EIMS of **5** showed a prominent fragment ion peak at *m/z* 336 due to $[M-C_5H_{10}]^+$ (**5b**) which was formed by retro-Diels–Alder reaction of the *p*-menthene residue [15, 22–24], also the ^{1}H and ^{13}C NMR spectral data corresponding to the *p*-menthene moiety were in good agreement with those of 1″-substituted *p*-menthene derivatives isolated previously [15, 22, 23]. The NOESY spectrum made it possible to clarify the position of the methoxyl group on the chalcone. The NOE was observed between H-5′ and the methoxyl group, and between H-1″ and the methoxyl group. Thus, the methoxyl group was confirmed to be linked to the C-4′ position. The spin–spin coupling (J = 10.0 Hz) shown by the H-1″ and H-6″ made a significant contribution to the assignment of its relative configuration, *trans*-orientated. The absolute configurations remain to be investigated. Accordingly, **5** was assigned to be 2′,6′-dihydroxy-4′-methoxy-3′-(3″-methyl-6″-methylethyl-2″-cyclohexenyl)chalcone.

Flavonoids bearing cyclic monoterpenoid are very rare in nature [15, 21–23] and **5** is a new naturally occurring compound. Further chemical examination of other Lauraceous plants is now under way in our laboratory.

EXPERIMENTAL

^{1}H NMR (400 MHz) and ^{13}C NMR (100.6 MHz): TMS as int. standard. Assignments of the NMR spectra were achieved on the basis of ^{1}H–^{1}H COSY, NOESY, ^{1}H–^{13}C COSY and ^{13}C DEPT spectra, and by correlation with the previously described compounds.

Plant material. Bark of *Lindera umberata* was collected in April 1986 from the botanical garden of this college. A voucher specimen is deposited at the herbarium of our college (88-002).

Extraction and isolation. After being cut into short lengths, the bark (fr. wt 1.7 kg) was extracted with MeOH (12 l) under reflux. The extract was concd to almost dryness under red. pres., and the crude residue, after dilution with H_2O, was extracted with $CHCl_3$. The $CHCl_3$ soln was repeatedly subjected to CC on silica gel with *n*-hexane–EtOAc and $CHCl_3$–EtOAc solvent systems to afford compounds **1**–**5**.

Compound **1**. Colourless needles (EtOH), 234 mg, mp 128–129°.

Compound **2**. Colourless needles (*n*-hexane–Me_2CO), 2.93 g, mp 97–98°, $[\alpha]_D^{23} \pm 0°$ ($CHCl_3$; *c* 0.48).

Compound **3**. Pale-yellow needles (MeOH), 643 mg, mp 195–197°, $[\alpha]_D^{23} \pm 0°$ ($CHCl_3$; *c* 0.64).

Compound **4**. Reddish-brown needles (*n*-hexane–EtOAc), 414 mg, mp 155–156°.

Compound **5**. A yellow amorphous powder, 41.9 mg, $[\alpha]_D^{20}$ +119.7° ($CHCl_3$; *c* 0.76); UV λ_{max}^{MeOH} nm (log ε): 214 (4.49), 308 sh (4.25), 343 (4.44); IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 2930, 2860 (CH), 1620 (C=O), 1570, 1550, 1490, 1440, 1410, 1380, 1325, 1280, 1215, 1150, 1135, 1100, 1085, 1025, 970, 810; EIMS *m/z* (rel. int.): 406.2159 $[M]^+$ (47), calcd for $C_{26}H_{30}O_4$: 406.2145, 363 (12), 336 (100), 321 (27), 359 (12), 217 (32), 195 (13), 179 (23), 167 (13), 149 (36), 138 (15), 136 (14), 131 (18), 121 (25), 103 (21); ^{1}H NMR ($CDCl_3$): δ14.04 (1H, *br s*, OH), 8.01 (1H, *d*, J = 15.6 Hz, H-β), 7.80 (1H, *d*, J = 15.6 Hz, H-α), 7.63 (2H, *dd*, J = 7.8, 2.0 Hz, H-2, 6), 7.44–7.35 (3H, H-3, 4, 5), 7.15 (1H, *br s*, OH), 6.09 (1H, *s*, H-5′),

5.51 (1H, *br s*, H-2″), 3.91 (1H, *br d*, $J = 8.9$ Hz, H-1″), 3.81 (3H, *s*, OMe), 2.23 (1H, *m*, H-4″a), 2.12 (1H, *m*, H-4″b), 1.83 (3H, *br s*, H-7″), 1.80 (1H, *m*, H-5″a), 1.62 (1H, *m*, H-6″), 1.50 (1H, *m*, H-8″), 1.40 (1H, *m*, H-5″b), 0.87 (3H, *d*, $J = 7.0$ Hz, H-9″ or H-10″), 0.83 (3H, *d*, $J = 6.8$ Hz, H-9″ or H-10″); ^{13}C NMR: Table 1.

Acetylation of **5**. A soln of **5** (6.8 mg) in Ac_2O–pyridine was allowed to stand at room temp. overnight. After addition of H_2O, the reaction mixture was extracted twice with $CHCl_3$. The organic layer was evapd off and the crude residue chromatographed on silica gel with *n*-hexane–Me_2CO (5:1) to provide a pale-yellow amorphous powder, 7.3 mg (**5a**). IR ν_{max}^{KBr} cm^{-1}: 2950 (CH), 1770 (C=O), 1660, 1640, 1600, 1570, 1440, 1360, 1330, 1190, 1105, 1070, 1040, 880, 760; EIMS *m/z* (rel. int.): 490.2330 $[M]^+$ (13), calcd for $C_{30}H_{34}O_6$: 490.2356, 448 (23), 447 $[M - MeCO]^+$ (42), 406 (30), 405 (80), 378 (38), 363 (21), 337 (26), 336 (100), 321 (31), 301 (11), 283 (13), 259 (13), 217 (33), 179 (39), 169 (27), 163 (25), 149 (28), 147 (28), 131 (55), 103 (36); ^{1}H NMR ($CDCl_3$): δ7.53, 7.38 (5H, H-2–6), 7.47 (1H, *d*, $J = 16.1$ Hz, H-β), 6.92 (1H, *d*, $J = 16.1$ Hz, H-α), 6.58 (1H, *s*, H-5′), 5.14 (1H, *br s*, H-2″), 3.82 (4H, OMe and H-1″, overlapping), 2.11, 2.03 (each 3H, *s*, OAc), 2.10–2.02 (2H, H-4″), 1.96 (1H, *m*, H-6″), 1.77 (1H, *m*, H-5″a), 1.64 (3H, *s*, H-7″), 1.46 (1H, *m*, H-8″), 1.35 (1H, *m*, H-5″b), 0.87 (3H, *d*, $J = 6.9$ Hz, H-9″ or 10″), 0.80 (3H, *d*, $J = 6.8$ Hz, H-9″ or 10″).

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