
 Communications to the Editor

[Chem. Pharm. Bull.]
35(2) 920-923 (1987)

TWO NOVEL FLAVANONES, METHYLLINDERATONE AND ISOLINDERATONE, FROM
LINDERA UMBELLATA THUNB. VAR. MEMBRANACEA (MAXIM.) MOMIYAMA

Kazuhiko Ichino, Hitoshi Tanaka, and Kazuo Ito*
Faculty of Pharmacy, Meijo University, Tenpaku-ku, Nagoya 468,
Japan

From the fresh leaves of Lindera umbellata Thunb. var. membranacea (Maxim.) Momiyama two new flavanones, methyllinderatone (1) and isolinderatone (2), were isolated. Their structures were established by chemical and spectroscopic means.

KEYWORDS — Lauraceae; Lindera umbellata var. membranacea; linderatin; linderatone; methyllinderatone; isolinderatone; flavanone; p-menthene

In a previous paper,¹⁾ we reported the isolation and the structural determination of a dihydrochalcone, linderatin (8), from Lindera umbellata Thunb. var. lancea Momiyama and a flavanone, linderatone (7), from Lindera umbellata Thunb. Both compounds are novel flavonoids having a p-menthene substituent. In the course of further investigation of the genus Lindera, we isolated two new flavanone derivatives, named methyllinderatone (1) and isolinderatone (2) from the fresh leaves of Lindera umbellata Thunb. var. membranacea (Maxim.) Momiyama. Here we describe the structure elucidation of these compounds.

Methyllinderatone (1), a viscous oil, $[\alpha]_D +68.6^\circ$ ($c=0.35$, CHCl_3), gave a bluish color with ethanolic ferric chloride and was positive to the magnesium-hydrochloric acid test. The molecular formula was determined to be $\text{C}_{26}\text{H}_{30}\text{O}_4$ by the high-resolution mass spectrum (m/z 406.2158). The ^{13}C -NMR spectrum indicated the presence of twenty-six carbons (Table I). Other spectra of this compound are: IR $\nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 3600, 1630, 1570, 1495; UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 232 (sh), 292, 341 ($\lambda_{\text{max}}^{\text{MeOH}+\text{AlCl}_3}$ nm: 315, 364); ^1H -NMR (CDCl_3) δ : 0.79, 0.84 (6H, d x 2, $J=7$ Hz, two 8"-Me), 1.66 (3H, br s, 1"-Me), 2.76 (1H, dd, $J=4$, 17 Hz, 3- H_{eq}), 3.10 (1H, dd, $J=13$, 17 Hz, 3- H_{ax}), 3.77 (3H, s, 7-OMe), 5.16 (1H, br s, 2"-H), 5.43 (1H, dd, $J=4$, 13 Hz, 2-H), 6.08 (1H, s, 6-H), 7.44 (5H, s, Ar-H), 12.34 (1H, s, 5-OH); CD ($c=0.012$, MeOH): $[\theta]_{310} +2.00 \times 10^3$, $[\theta]_{289} -6.32 \times 10^3$, $[\theta]_{255} +6.99 \times 10^3$.

The mass spectrum of 1 showed a molecular ion at m/z 406 indicating an increase of fourteen mass units in comparison with 7. This spectrum also had the characteristic peak at m/z 336 which was formed by the retro Diels-Alder reaction²⁾ of a p-menthene unit as in 7. The ^1H -NMR and ^{13}C -NMR spectra of this compound were very similar to those of 7 except for the signal due to a methoxyl function. These results suggest that 1 may be a 7-O-methyl ether of 7 (^1H -NMR

δ : 3.77 (7-OMe), 12.34 (5-OH)). And treatment of 7 with CH_2N_2 in ether afforded a monomethyl derivative which was identical with 1 in all respects. Therefore, the structure of methylinderatone is represented by the formula 1.

Next, isolinderatone 2, a viscous oil, $[\alpha]_D -67.1^\circ$ (CHCl_3 , $c=1.25$), gave a bluish color with ethanolic ferric chloride and was positive to the magnesium-hydrochloric acid test. The molecular formula was determined to be $\text{C}_{25}\text{H}_{28}\text{O}_4$ by the high-resolution mass spectrum (m/z 392.1975). The ^{13}C -NMR spectrum indicated the presence of twenty-five carbons (Table I). Other spectra of this compound are: IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3370, 1640, 1600, 1445; UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 222, 294, 325 ($\lambda_{\text{max}}^{\text{MeOH}+\text{AlCl}_3}$ nm: 218 (sh), 315, 384); ^1H -NMR (CDCl_3) δ : 0.55, 0.79 (6H, d x 2, $J=7$ Hz, two 8''-Me), 1.77 (3H, br s, 1''-Me), 2.75 (1H, dd, $J=4$, 17 Hz, 3-H_{eq}), 3.07 (1H, dd, $J=13$, 17 Hz, 3-H_{ax}), 3.66-3.92 (1H, m, 3''-H), 5.30 (1H, dd, $J=4$, 13 Hz, 2-H), 5.50 (1H, br s, 2''-H), 6.04 (1H, s, 6-H), 7.39 (5H, s, Ar-H), 12.34 (1H, s, 5-OH); CD ($c=0.333$, MeOH): $[\theta]_{308} +2.12 \times 10^3$, $[\theta]_{288} -9.42 \times 10^3$, $[\theta]_{248} +4.71 \times 10^2$.

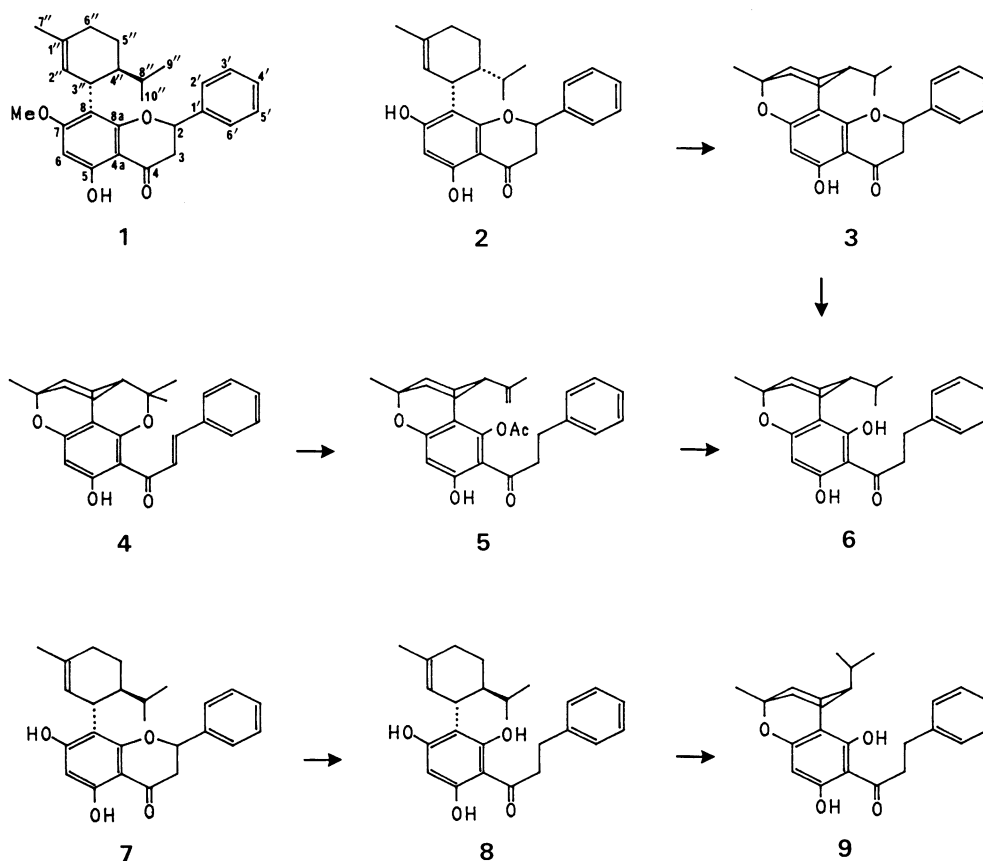


Chart 1

Table I. ^{13}C -NMR Chemical Shifts of 1, 2 and 7
 in Acetone- d_6

Carbon	1	2	7
C-2	80.1	79.9	79.7
C-3	43.8	43.8	43.7
C-4	197.4	197.5	196.7
C-4a	103.6	103.5	103.0
C-5	162.6*	165.6*	165.6*
C-6	92.1	96.8	95.8
C-7	167.4*	163.1*	163.3*
C-8	113.3	110.7	111.8
C-8a	162.2*	162.1*	161.7*
C-1'	140.1	140.2	139.9
C-2'	129.5	129.2	129.2
C-3'	127.3	129.1	127.1
C-4'	126.5	127.0	126.2
C-5'	127.3	129.1	127.1
C-6'	129.5	129.2	129.2
C-1''	132.5	133.5	134.0
C-2''	126.5	126.4	126.2
C-3''	35.9	36.3	35.7
C-4''	42.4	43.2	42.4
C-5''	23.6	23.5	23.6
C-6''	31.5	30.3	31.4
C-7''	23.9	23.5	23.9
C-8''	29.3	29.3	29.1
C-9''	16.7	16.7	16.7
C-10''	21.8	21.9	21.9
OMe	56.4	-	-

* Assignments may be interchanged.

Like 7, the mass spectrum of 2 showed a molecular ion at m/z 406. This spectrum also had a characteristic peak at m/z 322 which was formed by the retro Diels-Alder reaction of a *p*-menth-1-ene unit as in 1 and 7. The ^{13}C -NMR spectrum was similar to that of 7 except for a few signals assigned to the carbons of monoterpene unit (Table I). The ^1H -NMR spectrum also showed close similarity to that of 7 except for the chemical shifts of the geminal methyl groups. Comparison of the ^{13}C - and ^1H -NMR spectra of 2 with those of 5,7-dihydroxyflavanone also showed close similarity. This compound also seemed to be a 5,7-dihydroxyflavanone containing a monoterpene substituent on the A ring. The stereochemistry of its flavanone skeleton was the 2*S* configuration as in 7 according to the CD spectrum.³⁾ And the negative result of the Gibbs test and the bathochromic shift in the UV spectrum support the idea that 2 has a *p*-menth-1-ene group, not on the C-6 but on the C-8 position in the A ring, as mentioned^{1b)} about 7.

Next, from careful investigation by $^1\text{H-NMR}$ spectroscopy, we found that the signal of $\text{C}_3''\text{-H}$ was observed as multiplet⁴⁾ in 2, while it was found to be doublet in 7^{1b)} ($J_{3''\text{H},4''\text{H}} = 10 \text{ Hz}$) and 8^{1a)} ($J_{3''\text{H},4''\text{H}} = 12 \text{ Hz}$). This suggests that 2 might have been a C-4'' epimer (cis-isomer) of 7 concerning on the substitution pattern of the monoterpene unit. We already reported¹⁾ that hydrogenolysis of 7 followed by acid treatment of the resulting product 8 gave cyclolinderatin (9). Isolinderatone (2), the C-4'' epimer (cis-isomer) of 7, also can be converted into the corresponding dihydrochalcone 6 (C-4'' epimer of 9), which can be obtained from the readily available rubranin (4).⁵⁾

Thus, catalytic reduction of 4 with Pd-C in AcOEt followed by selective cleavage of the pyran ring with Ac_2O afforded an isopropenyl derivative 5. And compound 5 was transformed into the cis-isomer 6⁶⁾ by catalytic reduction and subsequent hydrolysis. Next, acid treatment of 2, followed by hydrogenolysis of the resulting cyclization product 3, gave a compound which was identical in all respects, not with 9 but with product 6 derived from 4.

Therefore, the structure of isolinderatone must be represented by the formula 2. It is particularly interesting that we could obtain the two epimers 2 and 7 from the same natural source.

REFERENCES AND NOTES

- 1) a) H. Tanaka, K. Ichino, and K. Ito, *Chem. Pharm. Bull.*, **32**, 3747 (1984);
b) idem, *ibid.*, **33**, 2602 (1985).
- 2) T. Nomura, T. Fukai, Y. Hano, K. Nemoto, S. Terada, and T. Kuramochi, *Planta Medica*, **47**, 151 (1983).
- 3) W. Gaffield, *Tetrahedron*, **26**, 4093 (1970).
- 4) In the $^1\text{H-NMR}$ spectrum of 7 or 8, the signal of $\text{C}_3''\text{-H}$ was observed as doublet ($J_{3''\text{H},4''\text{H}} = 10\sim 12 \text{ Hz}$) and no coupling was found between $\text{C}_2''\text{-H}$ and $\text{C}_3''\text{-H}$. Further investigation with molecular models (Dreiding models) revealed the fact that the dihedral angle between the two protons was approximately a right angle. On the other hand, the signal of $\text{C}_3''\text{-H}$ in 2 was observed as complicated pattern, in which the dihedral angle between $\text{C}_2''\text{-H}$ and $\text{C}_3''\text{-H}$ was not a right angle.
- 5) G. Combes, and Ph. Vassort, *Tetrahedron*, **26**, 5981 (1970).
- 6) The spectral data of 10 were as follows: high-resolution mass spectrum m/z : 394.2145 ($\text{C}_{25}\text{H}_{30}\text{O}_4$); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 3580, 1620; UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 228 (sh), 294; $^1\text{H-NMR}$ (CDCl_3) δ : 0.76, 1.14 (6H, d x 2), 1.33 (3H, s), 2.86-3.48 (4H, m), 5.66 (1H, s), 7.15 (5H, s), 13.76 (1H, s).

(Received December 23, 1986)