A NEW FLAVANONE, NEOLINDERATONE, FROM LINDERA UMBELLATA THUNB. VAR. LANCEA MOMIYAMA

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From the fresh leaves of Lindera umbellata Thunb. var. lancea Momiyama a new flavanone, named neolinderatone (**6**), was isolated and the structure was established by spectroscopic and chemical means as (2S,3"S,4"R,3"'S,4"'R)-5,7-dihydroxy-6,8-bis(4-isopropyl-1-methylcyclohex-1-en-3-yl)flavanone.

KEYWORDS Lauraceae; Lindera umbellata var. lancea; linderatin; linderatone; methyllinderatin; neolinderatin; neolinderachalcone; neolinderatone; flavanone; p-menthene

Previously, we reported[1-3] the isolation and the structural elucidation of five novel flavonoids, linderatin (**1**), linderatone (**2**), methyllinderatin (**3**), neolinderatin (**4**) and neolinderachalcone (**5**), having p-menthene substituents from the leaves of Lindera umbellata Thunb. var. lancea Momiyama. Further examination of the n-hexane extract of this plant led to the isolation of a novel flavanone derivative, named neolinderatone (**6**). The present paper describes the structure and the synthesis of this compound.

Neolinderatone (**6**), a viscous oil, $[\alpha]_D$ +22.0° (c=0.25, $CHCl_3$), gave a dark bluish color with ethanolic ferric chloride and was positive to the magnesium-hydrochloric acid test. The IR spectrum showed absorption bands for hydroxyl (3350 cm^{-1}) and conjugated carbonyl (1620 cm^{-1}) groups. The molecular formula was determined to be $C_{35}H_{44}O_4$ by the high-resolution mass spectrum (m/z 528.3264). In the ^{1}H-NMR spectrum ($CDCl_3$) of neolinderatone, signals of six methyl groups (δ 0.81, 0.82, and 0.84, 12H, d x 3, J=6.7 Hz, 8"- and 8"'-Me; δ 1.72 and 1.75, 6H, s x 2, 1"- and 1"'-Me), a methylene group (δ 2.80, 1H, dd, J=2.7, 17.1 Hz, 3-H_{eq}; δ 3.04, 1H, dd, J=13.5, 17.1 Hz, 3-H_{ax}), two benzylic methine protons (δ 3.78 and 3.88, 2H, br s x 2, 3"- and 3"'-H), a benzylic methine proton adjacent to an oxygen atom (δ 5.26, 1H, dd, J=2.7, 13.5 Hz, 2-H), two olefinic protons (δ 5.34 and 5.38, 2H, br s x 2, 2"- and 2"'-H), a hydroxyl group (δ 6.92, 1H, s, 7-OH), a phenyl group (δ 7.37-7.42, 5H, m), and a chelated hydroxyl group (δ 12.48, 1H, s, 5-OH) were observed. The ^{13}C-NMR spectrum was very similar to that of linderatone (**2**)[1] except for the signal of C-6 (δ 110.6, s) and the presence of the six signals (δ 17.1, 23.6, 28.9, 35.4, 125.4 and 139.1) assigned for another monoterpene unit (Table I). The mass spectrum of neolinderatone showed a molecular ion peak at m/z 528 indicating an increase of 136 mass units in comparison with that of **2**. This spectrum also had the characteristic fragmentation peak at m/z 458 (M^+-70) which was formed by the retro Diels-Alder reaction of a p-menthene unit as in **2**. These results suggest that neolinderatone should be a 6-terpenylated derivative of **2**, and the stereochemistry of its flavanone skeleton was fixed to the 2S configuration, as in **2**, according to the CD spectrum ($[\theta]_{290}$ -2.0×10^4).[1] Therefore, the structure of this compound appeared to be **6**.

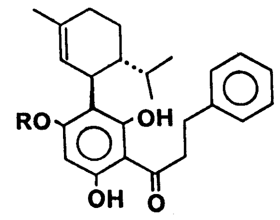
To confirm the structure and absolute configuration of neolinderatone, the following experiments were carried out. Treatment of 5,7-dihydroxyflavanone (100 mg) with (R)-(-)-α-phellandrene (53 mg) in the presence of p-toluenesulfonic acid (54 mg) in benzene at room temperature for 30 min gave a mixture of di-terpenylated derivatives (**6** and **6a**, 24 mg) and a mixture of mono-terpenylated derivative (**2** and **2a**, 32 mg).[4] The mixture (**6** and **6a**) was identical with neolinderatone in all respects (IR, UV and MS) except for the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of this mixture exhibited the signals superimposable on those of the natural specimen, but other signals (δ 0.75, 3H, d, J=6.7 Hz, 8"- or 8"'-Me; δ 2.78, 1H, dd, J=2.7, 17.1 Hz, 3-H_{eq}; δ 2.98, 1H, dd, J=13.5, 17.1 Hz, 3-H_{ax}) attributed to the 2-epi-derivative (**6a**) were also found.

Next, hydrogenolysis of the natural neolinderatone (5 mg) with Raney Ni (W-3) in EtOH afforded a dihydrochalcone derivative (2 mg; $[\alpha]_D$ +17.0°, $CHCl_3$, c 0.05) which was identical with neolinderachalcone (**5**)[3] in all respects (IR, ^1H NMR and $[\alpha]_D$). Therefore, the absolute structure of neolinderatone was established as (2S,3"S,4"R,3"'S,4"'R)-5,7-dihydroxy-6,8-bis(4-isopropyl-1-methylcyclohex-1-en-3-yl)flavanone (**6**). This is the first flavanone found to have two cyclic monoterpenes on the same benzene ring.

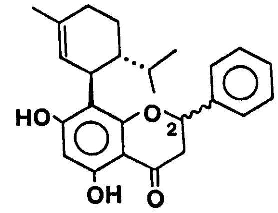
Table I. ^{13}C-NMR Chemical Shifts of 2 and 6 in $CDCl_3$

Carbon	2	6
C-2	79.1	78.9
C-3	43.5	44.2
C-4	195.9	196.5
C-4a	102.6	102.7
C-5	164.8[a)]	163.3[a)]
C-6	96.6	110.6
C-7	162.1[a)]	160.3[a)]
C-8	110.3	110.6
C-8a	161.2[a)]	158.9[a)]
C-1'	138.8	135.1
C-2'	128.9	128.6
C-3'	126.2	125.9
C-4'	126.2	125.7
C-5'	126.2	125.9
C-6'	128.9	128.6
C-1"	141.0	139.5[b)]
C-1"'	-	139.1[b)]
C-2"	124.5	125.1[c)]
C-2"'	-	125.4[c)]
C-3"	34.4	34.9[d)]
C-3"'	-	35.4[d)]
C-4"	44.1	42.7
C-4"'	-	42.7
C-5"	22.1	22.8
C-5"'	-	22.8
C-6"	30.7	30.9
C-6"'	-	30.9
C-7"	23.7	23.7[e)]
C-7"'	-	23.6[e)]
C-8"	28.0	28.4[f)]
C-8"'	-	28.9[f)]
C-9"	16.5	16.6[g)]
C-9"'	-	17.1[g)]
C-10"	21.8	21.6
C-10"'	-	21.6

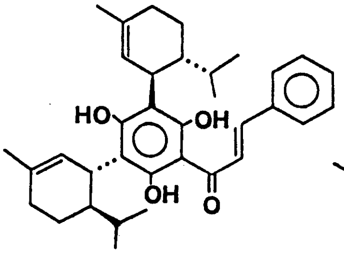
a-g) · Assignments may be interchanged in each column.



1: R=H
3: R=Me



2 : (2*S*)
2a: (2*R*)



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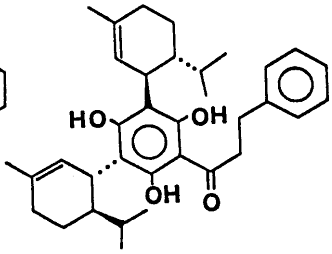

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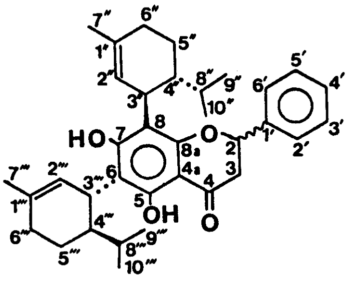

6 : (2*S*)
6a: (2*R*)

REFERENCES AND NOTES

1) K. Ichino, H. Tanaka, and K. Ito, Tetrahedron, **44**, 3251 (1988).
2) K. Ichino, Phytochemistry, **28**, 955 (1989).
3) K. Ichino, H. Tanaka, and K. Ito, Chemistry Letters, **1989**, 363.
4) Both mixtures (**2** and **2a**, and **6** and **6a**) were homogeneous on TLC behavior in a variety of solvent systems, respectively.

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