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A NOVEL FLAVANONE, LINDERATONE, FROM LINDERA UMBELLATA

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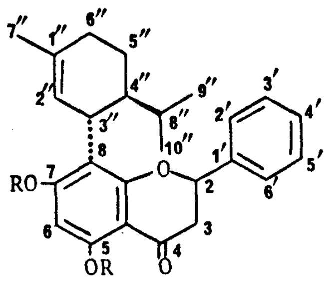
From the fresh leaves of Lindera umbellata Thunb. a new flavanone, named linderatone, was isolated. Its structure was established to be 1 by chemical and spectroscopic means.

KEYWORDS——Lauraceae; Lindera umbellata Thunb.; linderatin; linderatone; flavanone; p-menthene

In a previous paper,[1] we reported the isolation and the structural determination of a novel dihydrochalcone having a p-menthene substituent, linderatin (3), from Lindera umbellata Thunb. var. lancea Momiyama (Lauraceae). In extended studies of the genus Lindera, we isolated a new flavanone derivative, named linderatone (1), from the fresh leaves of Lindera umbellata Thunb. This paper deals with the structural elucidation of this compound.

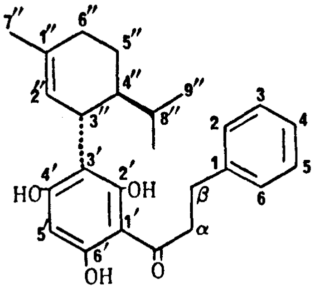
Linderatone (1), a viscous oil, $[\alpha]_D$ -25.6° (c=0.5, $CHCl_3$), gave a bluish color with ethanolic ferric chloride and was positive to the magnesium-hydrochloric acid test and the sodium borohydride test.[2] The molecular formula was determined to be $C_{25}H_{28}O_4$ by the high-resolution mass spectrum (m/z 392.1963). Acetylation of 1 with acetic anhydride in pyridine afforded a diacetate (2)[3] [oil; M^+, m/z 476; ^{1}H-NMR ($CDCl_3$) δ: 2.24, 2.34 (each 3H, 2 x s, 2 x $OCOCH_3$)]. Linderatone showed the following spectra: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370, 1635, 1620, 1580, 1450; UV λ_{max}^{MeOH} nm (log ε): 234 (sh, 4.06), 292 (4.06), 331 (sh, 3.45); ^{1}H-NMR (acetone-d_6) δ: 0.85, 0.88 (6H, 2 x d, J=7 Hz, 2 x CH_3), 1.67 (3H, br s, CH_3), 2.77 (1H, dd, J=4, 17 Hz, $C_{3\beta}$-H), 3.20 (1H, dd, J=12, 17 Hz, $C_{3\alpha}$-H), 3.87 (1H, br d, J=10 Hz, $C_{3''}$-H), 5.23 (1H, br s, $C_{2''}$-H), 5.56 (1H, dd, J=4, 12 Hz, C_2-H), 6.05 (1H, s, C_6-H), 7.4-7.7 (5H, m, 5 x aromatic protons), 9.15 (1H, br s, C_7-OH), 12.68 (1H, s, C_5-OH); MS m/z: 392 (M^+), 349, 322, 307, 270; CD (c=0.023, MeOH): $[\theta]_{312}$ +2.30 x 10^3, $[\theta]_{295}$ -1.36 x 10^4, $[\theta]_{256}$ +2.39 x 10^3. The mass spectrum of 1 displayed a molecular ion at m/z 392 which means there were two protons fewer than in that of 3. This spectrum also had a characteristic peak at m/z 322.1141 (4) which was formed by a retro Diels-Alder reaction[4] of a p-menthene unit, as in 3. Comparison of the ^{13}C-NMR spectrum of 1 with that of 3 showed that the chemical shifts of the carbon atoms of 1, except C-2, are similar to those of the relevant carbon atoms of 3. This indicates that 1 includes a p-menth-1-ene group as occurs in 3.

In the ^{1}H-NMR spectrum, the chemical shifts of the signals due to the flavanone skeleton are very similar to those of 5,7-dihydroxyflavanone pinocembrin (5) (δ 2.77, 3.20, 5.56, 6.05, 7.4-7.7, 9.15, and 12.68). Furthermore, in the ^{13}C-NMR spectrum, the chemical shifts of the carbon atoms of the dihydroxy-



1 : R=H

2: R=Ac



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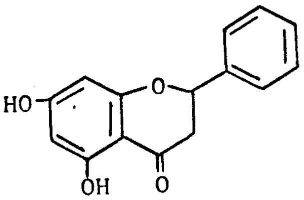

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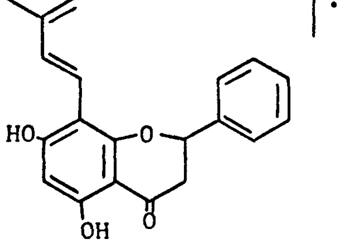
Table I. ^{13}C-NMR Chemical Shifts of 1, 3 and 5 in Acetone-$d_6$$^{a)}$ and DMSO-$d_6$$^{b)}$

Carbon	$1^{a)}$	$5^{b)}$	$3^{a)}$	Carbon
C-2	79.7	78.4	31.5	C-β
C-3	43.7	42.2	46.6	C-α
C-4	196.7	195.8	205.9	C=O
C-4a	103.0	101.9	105.4	C-1'
C-5	165.6*	163.6	165.9*	C-6'
C-6	95.8	96.1	95.8	C-5'
C-7	163.3*	166.6	163.9*	C-4'
C-8	111.8	95.1	110.5	C-3'
C-8a	161.7*	162.7	161.4*	C-2'
C-1'	139.9	138.0	143.2	C-1
C-2'	129.2	126.5	129.4	C-2
C-3'	127.1	128.5	129.6	C-3
C-4'	126.2	128.5	127.1	C-4
C-5'	127.1	128.5	129.6	C-5
C-6'	129.2	126.5	129.4	C-6
C-1"	134.0		135.4	C-1"
C-2"	126.2		126.9	C-2"
C-3"	35.7†		36.0†	C-3"
C-4"	42.4		43.0	C-4"
C-5"	23.6		23.7	C-5"
C-6"	31.4		31.5	C-6"
C-7"	23.9		23.7	C-7"
C-8"	29.1†		29.1†	C-8"
C-9"	16.7		16.9	C-9"
C-10"	21.9		22.0	C-10"

†,* Assignments may be interchanged.



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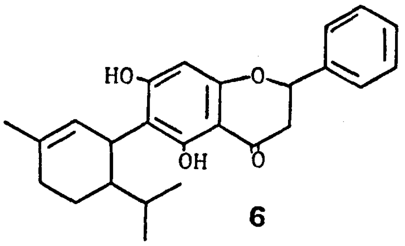

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flavanone skeleton, except those of C-6 or C-8, are also similar to those of the relevant carbon atoms of pinocembrin (5).[5] These results suggest that the A-ring of the dihydroxyflavanone skeleton is attached to the p-menth-1-ene moiety and this was further supported as follows. Hydrogenation of 1 with Raney nickel (W-3) in EtOH at room temperature for 4 h provided the optically active hydrogenated product (3) in 25% yield which was identical in all respects with an authentic sample.[1] Therefore, the stereochemistry at C-3" and C-4" of the p-menth-1-ene moiety on 1 is trans-oriented as in 3. This is also suggested by the large coupling constant ($J_{3''H,4''H}$=10 Hz) between the $C_{3''}$-H and $C_{4''}$-H in the ^{1}H-NMR spectrum. Two possible structures 1 and 6, regioisomers of the p-menth-1-ene group in the A-ring, are depicted for linderatone. The former was supported as follows. Linderatone was negative to the Gibbs test[6] and showed the bathochromic shift ($\lambda_{max}^{MeOH+AlCl_3}$ nm: 315 and 361) in the UV spectrum on the addition of aluminium chloride. It is known[7] that the aluminum chloride-induced shift in the UV spectra of 5-hydroxyflavanones occurs only in the absence of an alkyl substituent at C-6. Consequently, the structure of linderatone is represented by formula 1.

Finally, the CD spectrum of 1 exhibits the Cotton effects characteristic of 2S flavanones.[8] Furthermore, the large coupling constant ($J_{2Hax,\ 3Hax}$=12 Hz) between C_2-H and $C_{3\alpha}$-H indicates that the 2-phenyl ring exists in the equatorial position which is thermodynamically favourable.[9]

Linderatone is the third example[10] of a new class of compound which consists of a C_6-C_3-C_6 unit (flavonoid) and a cyclic monoterpene, and is the first natural product which has a flavanone skeleton as the C_6-C_3-C_6 unit.

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