CHEMISTRY LETTERS, pp. 1467-1468, 1993.

Aciculatalactone, A New Elemanolide Sesquiterpenoid from *Neolitsea aciculata* Koidz

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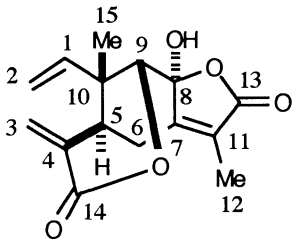
Two new elemanolides, aciculatalactone and de-*O*-methylsericealactone, have been isolated from *Neolitsea aciculata* Koidz. and their structures have been determined by using a variety of 2D NMR techniques and a X-ray crystallographic analysis.

We have already reported[1] the isolation and structure determination of two highly oxidized germacranolide sesquiterpene, neoliacine and neoliacine acid, with moderate cytotoxicity[2] in Hella cell culture *in vitro*, from the fresh leaves of *N. aciculata*, which is widely distributed in Japan. In continuing investigation on components of the above plant, we have isolated a new sesquiterpene dilactone alcohol, named aciculatalactone (**1**), and de-*O*-methylsericealactone (**2**) from leaves of the plant.



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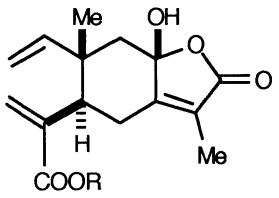

2: R=H
3: R=Me

Aciculatalactone (**1**), colorless needles from ethyl acetate, mp 175 °C (decomp), $[\alpha]_D$ +25° (c 0.1, C_5D_5N), UV (EtOH) 210 nm (ε 10000), has the formula $C_{15}H_{16}O_5$ deduced from high resolution mass spectrum (M^+ m/z 276.0986). The IR spectrum of **1** shows the presence of a hydroxyl group (3310 cm^{-1}), two lactone carbonyl groups (1755 and 1695 cm^{-1}) and olefinic double bonds (1635, 1620, 980, 965, and 920 cm^{-1}). The ^1H- and ^{13}C-NMR spectra of **1**, which were fully analyzed with the aid of ^1H-^1H and ^1H-^{13}C COSY, indicated the presence of an α-substituted- α,β-unsaturated γ-lactone [δ_C 171.24 (C-13), 153.16 (C-7), 129.12 (C-11), an α-methylene δ-lactone [δ_C 163.16 (C-14), 137.98 (C-4), 129.72 (C-3); δ_H 5.67 (1H, d, J=0.9 Hz), 6.59 (1H, d, J=1.2 Hz)], and a vinyl group [δ_C 141.47 (C-1), δ_H 6.58 (1H, dd, J=17.7 and 11.3 Hz); δ_C 111.30 (C-2); δ_H 5.18 (1H, d, J=17.7 Hz), 5.22 (1H, d, J=11.3 Hz) together with two methyl groups [δ_C 8.34 (C-12), δ_H 1.72 (3H, d, J=1.5 Hz); δ_C 25.44 (C-15), δ_H 1.14 (3H, s)], a methylene [δ_C 30.48 (C-6), δ_H 2.60 (1H, dd, J=4.3 and 14.0 Hz), 3.25 (1H, dm, J=14.0 Hz)], a methine [δ_C 43.65 (C-5), δ_H 3.22 (1H, br. s)] and an oxygenated methine [δ_C 85.46 (C-9), δ_H 4.84 (1H, br. s)]. In

considering these spectral data and molecular formula, **1** was assumed to be tricyclic sesquiterpene closely related to the known serisealactone (**3**).[3)]

The COLOC spectrum of **1** was measured in order to confirm the sequence of carbon atoms. The carbon signal at δ_C 43.65 (C-5) is correlated with the methyl protons at δ_H 1.14 (H-15) and the proton signal at δ_H 6.58 (H-3). Also, the carbon signals at δ_C 85.46 (C-9) and 141.47 (C-1) are correlated with the methyl protons at δ_H 1.14 (H-15). Furthermore, the carbonyl carbon signal at δ_C 171.24 (C-13) and the quaternary olefinic carbon signals at δ_C 129.12 and 153.16 are correlated with the methyl protons at δ_H 1.72 (H-12). Thus, the planar structure of this compound was shown to be **1**.

In order to further prove the relative stereochemistry of compound **1**, a single crystal X-ray diffraction experiment was performed; M_r = 276.10($C_{15}H_{16}O_5$), monoclinic, *Aa*, *a* = 13.338(6), *b* = 10.603(4), *c* = 9.399(3) Å and β = 92.58(3)°, *V* = 1327.9(9) Å^3, *Z* = 4, D_{calc} = 1.38 gcm^{-3}. All unique diffraction intensities with 2θ < 60.0° were collected in the variable speed ω-scan mode on a Mac Science MXC 18 four-circle automatic diffractometer using graphite monochromatised Mo-*K*α radiation (λ = 0.7107Å). Of the 2167 reflections collected, 1815 were judged to be observed after correction for Lorentz, polarization, and background effects. The structure was solved by direct methods using CRYSTAN program system. Full-matrix least-squares refinement with anisotropic temperature factors for the non-hydrogen atoms and isotropic factors for the hydrogen atoms converged to final *R* factor of 0.036 for the 1815 reflections.

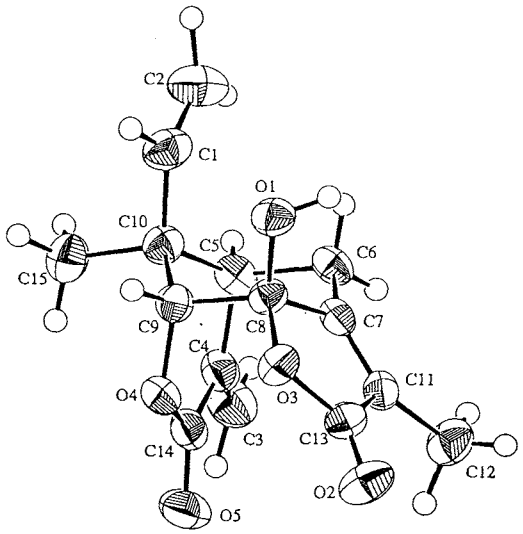

Fig. 1. ORTEP drawing of **1**.

Figure 1 shows a perspective drawing of the X-ray structure. Aciculatalactone thus has the stereochemistry shown in **1** having a unique lactone ring between C-14 and C-9, 8-OH configuration being opposite to that of sericealactone (**3**).

De-*O*-methylsericealactone (**2**), $C_{15}H_{18}O_5$, mp 280 °C, $[\alpha]_D$ 0° (c 1, C_5D_5N), UV (EtOH) 215 nm (ε 10000), contained a tertiary hydroxyl (3425 cm^{-1}; δ_C 104.1), a carboxyl (2300-3300 and 1695 cm^{-1}; δ_C 170.08), an α,β–unsaturated γ-lactone (1750 cm^{-1}; δ_C 121.19, 161.05, and 172.57), endo-methylene [1625 cm^{-1}; δ_H 5.76 and 6.71 (each 1H, s); δ_C 125.37 and 143.18] and a terminal vinyl groups [920 and 960 cm^{-1}; δ_H 4.96 (1H, dd, J=0.9 and 10.7 Hz), 5.07 (1H, dd, J=0.9 and 17.4 Hz), and 6.07 (1H, dd, J=10.7 and 17.4 Hz); δ_C 112.13 and 147.53)]. The above spectral data were almost idenical with those of sericealactone (**3**), previously isolated from *N. sericea*, except for the absence of a carbomethoxyl group signal.

References

1) H. Nozaki, M. Hiroi, D. Takaoka, and M. Nakayama, *J. Chem. Soc., Chem. Commun.*, **1983**, 1107; D. Takaoka, H. Nozaki, and M. Nakayama, *ibid*, **1987**, 1861.
2) Neoliacine at concentration 4 μg/ml inhibited the growth of Hella cells by 25%.
3) N. Hayashi, J. Sci. Hiroshima Univ., SER. A-II, **33**, 107 (1969).

(Received June 4, 1993)