Neoliacine, a Novel Germacranolide Sesquiterpene Dilactone from *Neolitsea acciculata* Koidz.: *X*-Ray Crystal Structure

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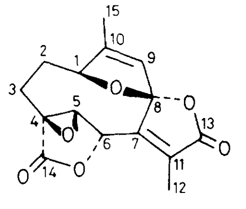
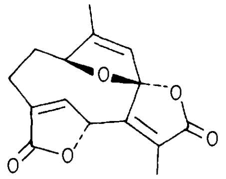
The structure and stereochemistry of neoliacine, a novel germacranolide sesquiterpene isolated from *Neolitsea acciculata* Koidz., have been elucidated on the basis of chemical transformation, spectral, and single-crystal *X*-ray analysis.

In continuing investigations on components of *Neolitsea acciculata* Koidz. (family of Lauraceae), we have isolated a new sesquiterpene dilactone, named neoliacine, from leaves of the plant. This compound exhibited moderate cytotoxicity in Hella cell culture *in vitro*. It was shown to have the structure and stereochemistry shown in (**1**) from chemical transformation, spectral,† and *X*-ray crystal structure analysis.

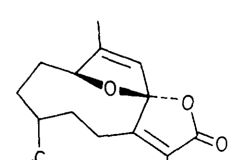
Neoliacine (**1**), $C_{15}H_{14}O_6$, M^+, m/z 290.0775, m.p. 283.0 °C (decomp.), $[\alpha]_D$ +7.3° (c 5.4, pyridine), was obtained as colourless crystals by repeated silicic acid chromatography. The presence of a γ-lactone and an α-substituted-α,β-unsaturated γ-lactone was indicated by i.r. (KBr) bands at ν 1785, 1760, and 1655 cm^{-1}, a u.v. (EtOH) absorption at 205 nm (ϵ 4000), and characteristic ^{13}C n.m.r. signals at δ 172.0 [s, C(14)], 169.0 [s, C(13)], 148.0 [s, C(7) or C(11)], and 147.2 p.p.m. [s, C(11) or C(7)]. The ^1H n.m.r. spectrum of (**1**) showed two vinyl methyl groups at δ 1.78 [3H, d, J 1.2 Hz, H(15)] and 1.95 [3H, s, H(12)], one of which was attached to a trisubstituted double bond [δ 5.16, 1H, br.s, H(9)] and the other to the α-position of the α,β-unsaturated γ-lactone. A low-field singlet at δ 5.08 was attributed to the γ-proton [H(6)] of the γ-lactone. These assignments were supported by ^{13}C n.m.r. signals at δ 8.5 [q, C(15)], 11.9 [q, C(12)], 71.1 [d, C(6)], 132.9 [s, C(10)], and 122.3 p.p.m. [d, C(9)]. The absence of a hydroxy group signal and the i.r. bands at ν 1100, 950, and 930 cm^{-1} suggested that the remaining two oxygen atoms must be present in ether functions, the existence of which was supported by signals at δ 4.66 [1H, s, H(5)] and 5.53 [1H, t-like, J 2.0 Hz, H(1)] in the ^1H n.m.r. and δ 60.2 [d, C(5)] and 87.8 p.p.m. [d, C(1)] in the ^{13}C n.m.r. spectra.



(**1**)



(**2**)



(**3**) R = H
(**4**) R = Me

On treatment with chromium(II) chloride, compound (**1**) was converted into the deoxy derivative (**2**), $C_{15}H_{14}O_5$, m.p. 140—141 °C, $[\alpha]_D$ +36.7° (c 4.9, $CHCl_3$), the spectra of which indicated the conversion of the original γ-lactone into an α,β-unsaturated γ-lactone (ν 1785 cm^{-1}, δ 5.9, 1H, s). This demonstrated that one of the ether functions in compound (**1**) belonged to a 1,2-epoxy group conjugated with the carbonyl group of the γ-lactone.[1] Hydrogenation of the deoxy derivative (**2**) in the presence of Pd–C (EtOH) yielded an oily dihydrocarboxylic acid (**3**), $C_{15}H_{18}O_5$, ν 1700 cm^{-1}, which was further converted into the methyl ester (**4**), $C_{16}H_{20}O_5$, m/z 292.1303, m.p. 144.5—146.5 °C, $[\alpha]_D$ +17.8° (c 2.0, $CHCl_3$). The cleavage of the γ-lactone by hydrogenation showed that the lactone oxygen was allylic to the olefinic bond.[2] This structural information suggested that neoliacine (**1**) was a germacranolide-type sesquiterpene which contained an ether function, an α-methyl-α,β-unsaturated γ-lactone, and one 1,2-epoxy ring conjugated with a carbonyl group of a saturated γ-lactone, together with a trisubstituted double bond bearing a methyl group.

The complete structure and stereochemistry of neoliacine were confirmed by single-crystal analysis. Crystals were orthorhombic, space group $P2_12_12_1$, a = 6.626(1), b = 7.700(1), c = 26.002(6) Å, D_c = 1.45 g cm^{-3}, Z = 4. All unique diffraction intensities with $2\theta \leqslant 55.0°$ were collected in the variable speed ω-scan mode on a Syntex R3 four-circle diffractometer with graphite-monochromated Mo-K_α radiation (0.7107 Å). Of the 1789 reflections collected, 1459 were judged to be observed after correction for Lorentz, polariza-

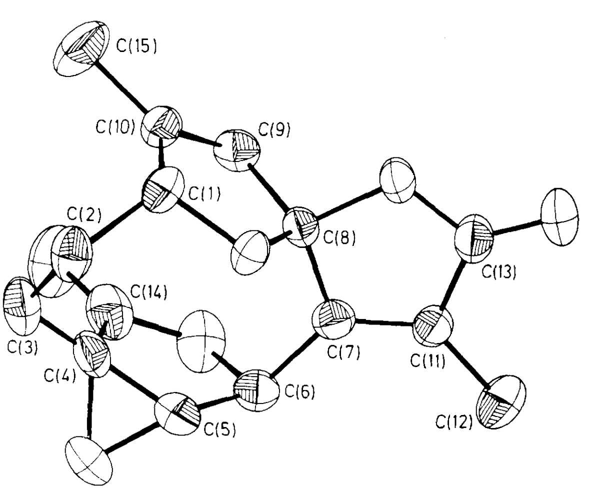


Figure 1. Perspective drawing of the *X*-ray structure of neoliacine (**1**).

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† ^{13}C and ^1H N.m.r. spectra of (**1**) were taken in $(CD_3)_2SO$ and C_5D_5N solution, respectively. All new compounds (**1**)—(**4**) gave spectral data in good agreement with the assigned structures.

tion, and background effects. The structure was solved by direct methods using MULTAN[3] in a Syntex XTL 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 a final *R* factor of 0.044 for the 1459 reflections.‡

Figure 1 shows a perspective drawing of the *X*-ray structure, and neoliacine thus has the stereochemistry shown in **(1)** having a unique ether linkage between C(1) and C(8). The distances and angles vary over a wide range and are different from the accepted values[4] because of the distortion caused by the fusion of two lactones and a five-membered ether ring. The five-membered ether ring and the γ-lactone ring bearing the epoxy function were parallel to each other and perpendicular to the ten-membered ring, the conformation of which could not be characterized by comparison with well known systems[5] in other compounds with ten-membered rings.

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‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.