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SALVIFARIN, X-RAY STRUCTURE DETERMINATION OF A *CIS* NEO-CLERODANE DITERPENOID FROM *SALVIA FARINACEA*

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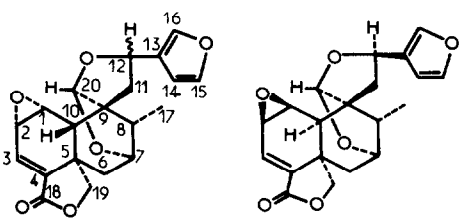
Key Word Index—*Salvia farinacea*; Labiatae; diterpenoid; *cis* neo-clerodane; salvifarin; revised structure.

Abstract—The structure and absolute configuration of salvifarin, a neo-clerodane diterpenoid isolated from *Salvia farinacea*, have been established by X-ray diffraction analysis. This result modifies the structure previously assigned to this compound.

In a previous communication [1] we reported the isolation and structure determination of two new diterpenoids, salvifarin and salvifaricin, from *Salvia farinacea* Benth. (Labiatae). On the basis of extensive ^1H and ^{13}C NMR spectroscopic studies we assigned structure **1** for salvifarin, but its configuration at the C-12 centre was suggested as 12*R* only on biogenetic grounds. This prompted us to obtain the X-ray diffraction molecular structure of salvifarin to definitely establish this point. Figure 1 shows the X-ray absolute molecular structure of the diterpenoid, in which the configuration at C-12 is *R*, as it was put forward earlier [1], but the configurations of the C-10 hydrogen atom and of the C-1, C-2-oxirane ring are opposite to those previously reported [1]. Thus, salvifarin possesses the structure of *cis* neo-clerodane depicted in formula **2**. Its ring A is roughly between a half-chair and twist conformation, whereas ring B has a chair distorted to envelope conformation. The conformational parameters of salvifarin (**2**) have been calculated in the same way as those reported [2] for some neo-clerodane diterpenoids, and these values are: $\theta_A = 114°$, $\phi_A = 91°$, $Q_A = 0.32$ Å; $\theta_B = 28°$, $\phi_B = 303°$ and $Q_B = 0.67$ Å.

It is important to note that although salvifarin (**2**) is a *cis* neo-clerodane diterpenoid, and its C-19 methylene and C-20 acetal hydrogen atoms are more distant than in a *trans* neo-clerodane structure, there exists a strong NOE between these protons [1].



1 **2**

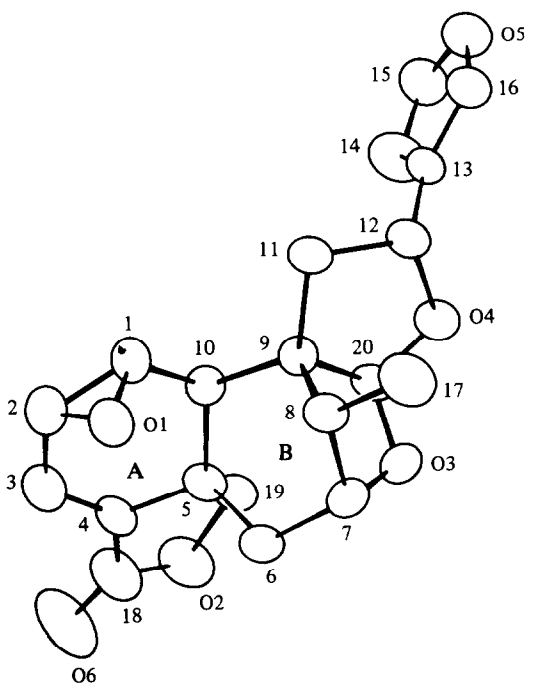


Fig. 1. X-ray molecular model of salvifarin (**2**).

EXPERIMENTAL

For isolation of salvifarin (**2**) from *Salvia farinacea* and its spectroscopic data, see ref. [1].

X-ray structure determination of salvifarin (**2**). Crystals of salvifarin ($C_{20}H_{20}O_6$) are orthorhombic, $P2_12_12_1$, $Z = 4$, with $a = 20.988$ (2), $b = 9.280$ (1) and $c = 8.6088$ (4) Å, $D_c = 1.412$ g/cm^3 and $\mu = 8.24$ cm^{-1}. Graphite-monochromatic CuKα radiation ($\lambda = 1.5418$ Å) was selected to measure the intensity of the 1733 independent Friedel pairs up to $\theta = 67°$, on a crystal of 0.16 × 0.22 × 0.24 mm. With the aid of an automatic diffractometer, each reflexion was scanned 1.2° in 0.5 min, by the $\omega/2\theta$ mode, and individual background was also measured. No intensity decay was observed during the experiment. The crystal

structure was solved by MULTAN [3], with the 254 E's > 1.42. After refinement with the 1555 $2\sigma(I)$ observed intensities and location of the hydrogen atoms on a difference map, a weighting scheme was selected to have no dependence of $\langle w\Delta^2F\rangle$ vs. $\langle F_o\rangle$ and vs. $\langle \sin\theta/\lambda\rangle$. A weighted full matrix L.S. anisotropic refinement (fixed isotropic for H atoms) using the 1555 observed Friedel pairs converged to $R = 4.5\%$ and $R_w = 5.7\%$ [4].

The neo-clerodane absolute configuration of salvifarin (Fig. 1 and 2) was determined comparing the 84 Bijvoet pairs with $\Delta F_c > 0.08$ and with less experimental error, that is $F_o > 10\sigma(F_o)$, $4 < F_o < 25$ and $0.22 < \sin\theta/\lambda < 0.58$. The averaged Bijvoet difference was 0.359 for the right enantiomer vs. 0.434 for the wrong one*.

*A list of atomic parameters, bond distances and angles, torsion angles and $F_o - F_c$ tables are deposited at the Cambridge Crystallographic Data Centre.

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A COUMARIN ACETYLGLUCOSIDE FROM *VIBURNUM SUSPENSUM*

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Key Word Index—*Viburnum suspensum*; Caprifoliaceae; coumarin; 2′,6′-*O*-diacetylscopolin.

Abstract—A new acetylated coumarin glucoside has been isolated from the leaves of *Viburnum suspensum* and determined as 2′,6′-*O*-diacetylscopolin on the basis of spectral and chemical evidence.

INTRODUCTION

Recently, we have isolated two known flavonol glycosides [1] and several bitter iridoids [2] from the leaves of *Viburnum suspensum* L. Further chromatographic examination of the leaves of the plant gave a new acetylcoumarin glucoside (**1**).

RESULTS

Compound **1** was crystallized as needles, mp 178–179.5°, $[\alpha]_D^{25}$ −100° from methanol. The molecular formula $C_{20}H_{22}O_{11}\cdot 1/2\ H_2O$ was determined on the basis of the elementary analysis and mass spectrum. Absorption bands at 1740, 1620 and 1570 cm^{-1} in the IR spectrum and absorption maxima at 227 nm (ε10800), 286 nm (ε5600) and 328 nm (ε7600) in the UV spectrum suggested that **1** is a coumarin. Additional evidence for the presence of this carbon skeleton came from the ^{1}H NMR spectrum. The signals corresponding to C-3 and C-4 protons appeared as an AB system at δ6.30 and 7.63 (J = 9.8 Hz). Two singlets at δ7.00 and 7.38 (1H each) were attributable to C-8 and C-5 protons, respectively. The ^{1}H NMR spectrum also showed the presence of two acetyl groups at δ2.07 (3H × 2, *s*) and one methoxyl group at δ3.70 (3H, *s*).

On acetylation with acetic anhydride–pyridine, **1** gave a tetra-acetate (**2**), mp 168–169°, $C_{24}H_{26}O_{13}$. The physical and spectral data of **2** [ν_{max}^{nujol} cm^{-1}: 1770–1730, 1620, 1570, 1505, 920, 890 and 825; δ2.10 (3H × 3, *s*), 2.17 (3H, *s*), 3.95 (3H, *s*), 7.20, 7.40 (1H each, *s*), 6.38 and 7.95 (1H each, *d*, J = 10 Hz)] were identical with those of scopolin acetate [3].

Therefore, two acetyl groups in **1** are located in the glucosyl moiety, and their positions were determined by detailed analysis of the ^{1}H NMR spectrum of **1** with aid of decoupling procedures. A doublet at δ5.43 (1H, J = 8.5 Hz) was assigned to an anomeric proton, which was coupled with a C′-2 proton at δ5.68 (1H, *dd*, J = 8.5 and 8.5 Hz). On irradiation at δ5.68, a double doublet at δ4.23 (1H, *dd*, J = 8 and 8.5 Hz) due to a C′-3 proton collapsed