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THE CORRECT STRUCTURE OF SALVIFARICIN, A *CIS* NEO-CLERODANE DITERPENOID FROM *SALVIA FARINACEA*

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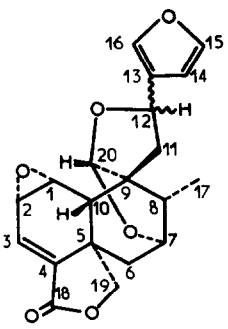
Key Word Index—*Salvia farinacea*; Labiatae; diterpenoid; *cis* neo-clerodane; salvifaricin; revised structure.

Abstract—The structure and absolute configuration of salvifaricin, a neo-clerodane diterpenoid isolated from *Salvia farinacea*, have been firmly established by extensive NOE experiments and by chemical correlation with salvifarin, another diterpenoid isolated from the same source. These results slightly modify the structure previously assigned to the compound.

In a previous communication [1] we reported the isolation of two new diterpenoids, salvifarin and salvifaricin, from *Salvia farinacea* Benth. (Labiatae) and, on the basis of ^{1}HNMR and ^{13}CNMR spectroscopic studies, we assigned structures **1** and **2**, respectively, for these neo-clerodane derivatives. Afterwards, an X-ray diffraction analysis of salvifarin established that its correct structure was **3** instead of **1** [2], thus forcing us to reconsider the structure **2** previously assigned to salvifaricin [1] and, in particular, the configuration of its C-10 and C-12 asymmetric centres.

Since the structure and absolute configuration of salvifarin (**3**) are well-known by its X-ray diffraction analysis [2], we have now performed a comparative study between this compound (**3**) and salvifaricin in order to establish the relative arrangement of the C-10, C-12, C-17 and C-20 protons of the latter using NOE experiments. Irradiation of the broad singlet of H-10 at δ 2.10 in salvifarin (**3**) produced a strong NOE enhancement (~ 20%) on the H-20 singlet at δ 5.28, and *vice versa*. The same NOE enhancements between the signals at δ 2.76 (H-10) and 5.19 (H-20) were observed in salvifaricin (**4**), thus confirming the same relative arrangement of H-10 and H-20 in both compounds and, consequently, an AB *cis* neo-clerodane structure of salvifaricin (**4**). The irradiation of the Me-17 signal at δ 1.38 in salvifarin (**3**) produced an 8% NOE enhancement on the H-12 triplet at δ 5.37. This effect was not observed in related neo-clerodane derivatives in which the configuration at C-12 was *S*, owing to the greater distance between the H-17 and H-12 protons in the latter compounds (a more detailed discussion of this point will be the subject of a forthcoming publication). The irradiation of the Me-17 signal at δ 1.37 in salvifaricin (**4**) also gave rise to an 8% NOE enhancement on the H-12 triplet at δ 5.28. This established the configuration *R* at C-12 for salvifaricin (**4**). It is important to mention that in both salvifarin (**3**) and salvifaricin (**4**) a strong NOE enhancement (20%) was observed on the C-19 protons when the signal of the acetalic proton (H-20) was irradiated. This effect was one of the reasons that led us wrongly to postulate originally an AB *trans* neo-clerodane structure for these two compounds [1]. Thus, the structure and relative stereochemistry of salvifaricin are the ones depicted in formula **4** (see also ref. [1]).

Finally, all the above deductions were confirmed and a



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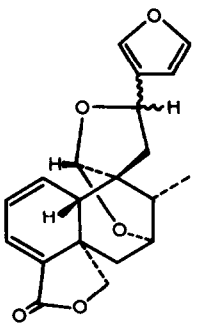

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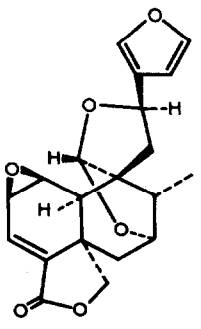

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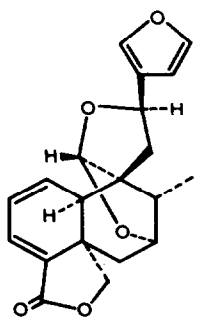

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neo-clerodane [3] absolute configuration of salvifaricin (4) was established by the fact that treatment of salvifarin (3) with sodium iodide-*p*-toluensulfonic acid in acetonitrile solution [4] yielded a compound identical in all respects (mp, mmp, $[\alpha]_D$, IR, ^{1}H NMR, mass spectra, TLC) with natural salvifaricin (4).

EXPERIMENTAL

For the isolation of salvifaricin (4) from *Salvia farinacea* and its spectroscopic data see ref. [1]. ^{1}H NMR spectra were measured at 80 MHz in $CDCl_3$ soln with TMS as internal standard. The proton NOE measurements were made by the FT difference method with the decoupler operating in the gated mode.

Salvifaricin (4) *from salvifarin* (3). A mixture of salvifarin (3, 36 mg, 0.1 mmol), NaI (0.5 mmol) and *p*-toluensulfonic acid (0.3 mmol) in dry acetonitrile (1 ml) was stirred at room temp. for 1 hr. Work-up in the usual manner [4] yielded, after preparative TLC purification, 28 mg of a compound, mp 213–215° (from MeOH), $[\alpha]_D^{22}$ −153.7° ($CHCl_3$; *c* 0.37), identical in all respects (mmp, IR, ^{1}H NMR, mass spectra, TLC) with salvifaricin (4, mp 214–215°, $[\alpha]_D^{20}$ −155.2°) [1].

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THE STRUCTURE OF SAGITTARIOL*

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Key Word Index—*Sagittaria sagittifolia*; Alismataceae; sagittariol; oxodeoxysagittariol; methyl hardwickiate; hardwickiol; kolavenic acid; methyl floribundate; cistodiol; ^{13}C NMR spectra.

Abstract—Sagittariol, heretofore considered to be 17-hydroxymanool, has been shown to incorporate an A-B *cis* clerodane skeleton on the basis of a ^{13}C NMR spectral analysis of several labdanic and clerodanic diterpenes.

In a recent study of sagittariol, a chemical constituent of the Indian aquatic herb *Sagittaria sagittifolia* L., the compound was assigned the labdane structure **1a**, on the basis of ^{1}H NMR (60 MHz) and mass spectral data and some chemical transformations [1]. However, a NMR reinvestigation now has yielded evidence incompatible with this formulation. Firstly, a ^{1}H NMR spectral analysis at 360 MHz has revealed the diterpene's four methyl groups as three singlets and one doublet, indicative of a methyl function residing on a methine. Secondly, ^{13}C NMR spectral comparison of sagittariol with its cogener oxodeoxysagittariol [J. S. Tandon, unpublished observations], initially formulated as **1b**, showed the strongly deshielded keto-α-carbon of the latter to be a methylene instead of a methine. In addition, the chemical shifts of the octalone carbons of the latter ketone were strikingly different from those of hedychenone (2) [2], an oxolabdane of related structure.

Sagittariol and its 14,15-dihydro product exhibited carbon signals characteristic of the methylvinylcarbinol terminus of the C-9 side-chain of manool [3]. Comparison of the carbon shifts of the nuclear double bond and the hydroxymethyl group of sagittariol with those of the product of acetylation of the primary alcohol moiety revealed $\Delta\delta$ values indicative of a second allyl alcohol unit in the diterpene [4]. Whereas all functional groups had been recognized correctly previously [1], they could not

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