

NEW DITERPENES FROM *SALVIA PACHYSTACHYS*

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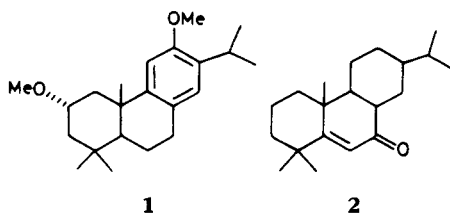
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ABSTRACT.—Two new diterpenes, 2 α -hydroxyferruginyl-2,12-dimethyl ether and pachystazone (abiet-5-en-7-one) were isolated from *Salvia pachystachys* together with the known diterpenes cryptanol, taxodione, royleanone, horminone, sugiol, 15-hydroxyferruginol, and ferruginyl-12-methyl ether. The structures of the compounds were established by spectral methods.

As a part of our continuing chemical investigations of Turkish *Salvia* species we have now examined *Salvia pachystachys* Trautv. (Labiatae). Nine abietane-type diterpenes were obtained, seven of which are known compounds: cryptanol (1), horminone, royleanone (2), sugiol (3), 15-hydroxyferruginol (4), taxodione (5), and ferruginyl-12-methyl ether (6). The other two are new, 2 α -hydroxyferruginyl-2,12-dimethyl ether [**1**] and pachystazone (abiet-5-en-7-one) [**2**]. The structures of the new diterpenoids were determined from spectral data.

2 α -Hydroxyferruginyl-2,12-dimethyl ether [**1**] exhibited uv and ir spectra similar to those of ferruginol and ferruginyl-12-methyl ether. The mass spectrum of **1** gave a molecular ion peak at m/z 330, indicating a molecular formula $C_{22}H_{34}O_2$, which was confirmed by its elemental analysis. The 1H -nmr spectrum was similar to that of ferruginyl-12-methyl ether except for the presence of a signal for a second methoxyl group at δ 3.77. The signal at δ 3.8 (1H, dddd, $J = 5$ Hz, 9 Hz, 5 Hz, 9 Hz) indicated that the second

methoxyl group could be located either on ring A or ring B. In the case of ring B there were two possibilities for its position, C-6 or C-7. If it were at C-6 the methyl group at C-10 would exhibit a chemical shift at ca. 1.60–1.70 ppm (7–9), while if it were at C-7 the chemical shift of the benzylic proton would be around 4.5–4.8 ppm (10). Because signals with these chemical shifts were not observed, it should be in ring A. There are three possible positions for the methoxyl group in ring A; C-1, C-2, or C-3. Although the splitting pattern of the signal at δ 3.80 indicated that it should be situated between two methylene groups, this position was confirmed by spin-decoupling experiments. When the signal at δ 3.80 (H-2) was irradiated, the broad doublet at δ 2.8 (1H, br d, $J = 15$ Hz, H-1 β) became a sharp doublet and the double doublet at δ 2.47 (1H, dd, $J = 13$ Hz and 5 Hz, H-3 β) collapsed to a doublet. When the signal at δ 2.8 (H-1 β) was irradiated, the signal at δ 3.80 (H-2) became a broadened triplet, while no change was observed in the signal at δ 2.47 (H-3). The second methoxyl group should therefore be at C-2. The stereochemistry of this group was determined to be α by measuring the J values ($J_{2a,1e} = J_{2a,3e} = 5$ Hz, $J_{2a,1a} = J_{2a,3a} = 9$ Hz) and by studying a Dreiding model. The spectral data suggested that **2** has the given structure.



The mass spectrum of pachystazone [2] gave a molecular ion peak at m/z 288, which together with elemental analysis indicated a molecular formula $C_{20}H_{32}O$. A strong band at 1685 cm^{-1} in the ir spectrum of 2 indicated the presence of an α,β -unsaturated ketone, and a uv maximum at 237 nm supported the presence of a conjugated carbonyl group. Biogenetic considerations and the ^1H -nmr spectrum provided information that established an abietane structure for 2 (7,8). There were five methyl signals, which appeared as singlets at δ 0.80, 0.82, 1.17 and as doublets at δ 0.81, 0.85. The presence of a methine proton signal between δ 2.2 and 2.5 as a multiplet together with the signals for H-12, H-13, H-14 indicated that the compound possessed a saturated C ring. Because only one vinylic proton signal was present at δ 5.72 (1H, d, $J = 1.5\text{ Hz}$) (long range coupling) there could be only three possible positions for the enone group: 7-en-6-one, 5-en-7-one, or 9(11)-en-12-one. The first position, 7-en-6-one, would cause a downfield shift of the signal for C-10 methyl group to around 1.3 ppm (11), but none of the methyl signals were in this area. In order to decide for one of the two other positions, nOe experiments were performed. When the signal at δ 5.72 was irradiated, nOe was observed only in the methyl signals at δ 0.80–0.85. Because there is no nOe present between the signals at 2.0 (H-1 β) and at δ 5.72, nor with the signal of the multiplet at δ 2.2–2.5 (H-12, H-13, H-14, H-15), the possibility of a 9(11)-en-12-one position for the enone was ruled out, and the structure of 2 must be abiet-5-en-7-one. The ^{13}C -nmr spectrum showed the unsaturated carbonyl at 198.0 ppm and the unsaturated carbon atoms at 159.1 (C-5) and 125.2 (C-6).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv spectra were recorded on a Varian Techtron 635 spectrophotometer in Et_2O , ir on a Perkin-

Elmer 577 in CHCl_3 , ^1H nmr on a Bruker FT 200 MHz, ^{13}C nmr on a Bruker FT 50.323 MHz in CDCl_3 , and ms on a Varian MAT 711. Kieselgel 60 F 254 (E. Merck) tlc plates were used for preparative separation.

PLANT MATERIAL.—The aerial parts of *S. pachystachys* were collected from central Turkey (Koramas mountain, Kayseri) in July 1988, and identified by one of us (Dr. E. Tuzlaci). A voucher specimen was deposited in the Herbarium of the Faculty of Pharmacy, University of Marmara (MARE 1608).

EXTRACTION AND FRACTIONATION.—The powdered plant material (540 g) was extracted in a Soxhlet with light petroleum ether followed by Me_2CO . Both extracts showed similar spots on tlc plates, so they were combined. The combined extract (13 g) was fractionated on a Si gel (70–230 mesh) (E. Merck) column (4 \times 60 cm). The column was eluted with light petroleum ether, and a gradient of Et_2O was added up to 100%, followed by EtOH to 10%. Diterpenoids were obtained in the following order: cryptanol (70 mg), taxodione (50 mg), royleanone (17 mg), horminone (140 mg), ferruginyl-12-methyl ether (6 mg), 2 α -hydroxyferruginyl-2,12-dimethyl ether (10 mg), sugiol (10 mg), and pachystazone (7 mg). Flavonoids (2.2 g) and a crude mixture of triterpenic compounds (550 mg) were not investigated.

The known compounds were identified by comparing their spectra with those of authentic samples and, except for taxodione, by tlc comparisons. NOe experiments, in addition to other spectral methods, assisted in the structure assignment of taxodione.

2 α -HYDROXYFERRUGINYL-2,12-DIMETHYL ETHER [1].—Pale yellow compound; mp 92° (crystals from MeOH); uv λ max (Et_2O) nm (log ϵ) 283 (sh), 280 (4.0), 228 (4.5); ir ν max (CHCl_3) 3040, 2960, 1625, 1610, 1580, 1550, 1450, 1230, 1020 cm^{-1} ; ^1H nmr (CDCl_3) δ 6.91 (1H, s, H-11), 6.65 (1H, s H-14), 3.74 (3H, s, OMe), 3.77 (3H, s, OMe), 3.11 (1H, septet, $J = 7\text{ Hz}$, H-15), 3.80 (1H, dddd, $J = 5\text{ Hz}$, 9 Hz, 5 Hz, 9 Hz, H-2 β), 2.80 (1H, br d, $J = 15\text{ Hz}$, H-1 β), 2.47 (1H, dd, $J = 13\text{ Hz}$ and 5 Hz, H-3 β), 1.17 (3H, d, $J = 7\text{ Hz}$), 1.16 (3H, d, $J = 7\text{ Hz}$) (H-16 and H-17), 0.97 (3H, s, H-20*), 0.87 (3H, s, H-19*), 0.85 (3H, s, H-18*) (assignments marked with an asterisk are interchangeable); eims m/z (rel. int.) $[\text{M}]^+$ 330 ($\text{C}_{22}\text{H}_{34}\text{O}_2$) (95), $[\text{M} - \text{Me}]^+$ 315 (20), $[\text{M} - 2 \times \text{Me}]^+$ 300 (12), $[\text{M} - 3 \times \text{Me}]^+$ 285 (100), 215 (20), 189 (42), 97 (20), 83 (50), 69 (80), 55 (80). Found C 79.88, H 10.27; calcd for $\text{C}_{22}\text{H}_{34}\text{O}_2$, C 80.00, H 10.33%.

PACHYSTAZONE (ABIET-5-EN-7-ONE) [2].—

Colorless, amorphous compound: uv λ max (Et₂O) nm (log ϵ) 237 (4.2); ir ν max (CHCl₃) 2960, 2945, 2880, 1685, 1617, 1460, 1380, 1270, 1230, 1180, 860 cm⁻¹; ¹H nmr (CDCl₃) δ 5.72 (1H, d, J = 1.5 Hz, H-6), 2.0 (1H, ddd, J = 15 Hz, 12 Hz, 4 Hz, H-1 β), 2.2–2.5 (4H, m, H-12, H-13, H-14, H-15), 1.17 (3H, s, H-20*), 0.82 (3H, s, H-19*), 0.80 (3H, s, H-18), 0.81 (3H, d, J = 7 Hz), 0.85 (3H, d, J = 7 Hz) (H-16 and H-17) (assignments with an asterisk are interchangeable); ¹³C nmr (CDCl₃) 36.1 (C-1), 18.9 (C-2), 35.6 (C-3), 37.8 (C-4), 159.1 (C-5), 125.2 (C-6), 198.0 (C-7), 35.2 (C-8), 35.2 (C-9), 37.8 (C-10), 18.9 (C-11), 33.4 (C-12), 36.4 (C-13), 28.6 (C-14), 37.0 (C-15), 23.2 (C-16*), 23.2 (C-17*), 24.6 (C-18*), 18.4 (C-19*), 24.6 (C-20*) (assignments with an asterisk are interchangeable); eims m/z (rel. int.) [M]⁺ 288 (C₂₀H₃₂O) (14), [M – Me]⁺ 273 (8), [M – CO]⁺ 260 (6), 175 (20), 133 (50), 107 (92), 95 (100), 83 (72), 69 (76). Found C 83.12, H 11.04; calcd for C₂₀H₃₂O, C 83.33, H 11.11%.

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