STRUCTURES OF FERTENIDIN AND FERTENICIN

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Two new esters have been isolated from the roots of Ferula tenuisecta by column chromatography: fertenidin, $C_{22}H_{32}O_5$, mp 236-238°C, $[\alpha]_D$ +145° (c 0.5; ethanol) and fertenicin, $C_{22}H_{30}O_4$ (amorphous), and the following most probable structures have been suggested for them: 6,10-dihydroxy-8-(p-hydroxybenzoyl)germacr-4(14)-ene and 10-hydroxy-8-(p-hydroxybenzoyl)germacra-4,6-diene, respectively.

Among the species of plants of the genus Ferula studied, Ferula tenuisecta is distinguished by a qualitative diversity of the esters that it contains. Eight esters of sesquiterpene alcohols of the daucane, germacrane, and guaiane series have been isolated from the roots and fruit of this plant [1-5]. Studying roots collected in the upper reaches of the R. Angren (Tashkent province) we have isolated two more esters differing in their physicochemical characteristics from those already known, and we have called them fertenidin (I) and fertenicin (II).

Fertenidin is a crystalline substance with the composition $C_{22}H_{32}O_5$, soluble in ethanol and pyridine. Its UV spectrum shows an absorption maximum at 260 nm (log ε 3.6), the bathochromic shift of which when the spectrum is recorded with the addition of alkali is characteristic for a p-hydroxybenzoyl chromophore. The good solubility of the substance in aqueous solutions of alkalis with the formation of phenolates confirmed the presence of a hydroxybenzoyl residue.

According to its IR spectrum, the fertenidin molecule includes the following functional groups: an exomethylene group (885, 1610 cm^{-1}), [6], and ester carbonyl attached to an aromatic ring (1050, 1280, 1680 cm^{-1}), a hydroxy group (3200-3600 cm^{-1}), and also an aromatic nucleus (1520, 1590, 1610 cm^{-1}). The PMR spectrum of (I) confirmed the presence of these groupings: the protons of the exomethylene group gave signals at 4.86 and 5.18 ppm – broadened singlets of 1 H each; the gem-hydroxylic proton gave a one-proton quartet at 4.15 ppm (J_1 = 10.5 Hz, J_2 = 5 Hz) and the gem-acyl proton gave a multiplet at 5.35 ppm (1 H). Two doublets of 2 H each at 6.84 and 7.88 ppm with the same spin–spin coupling constant (SSCC), J = 9 Hz, were due to four ortho-interacting protons of an aromatic nucleus. In addition to this, the signals of the following protons were observed in the strong field: those of isopropyl groups at 0.81 ppm (6 H, t, $J_1 = J_2$ = 6 Hz); of a methyl group of a carbon atom bearing an oxygen-containing functional group at 1.15 ppm (3 H, s); and of methylene protons at 2.65 ppm (2 H, d, J = 5 Hz).

The acetylation of fertenidin with acetic anhydride in pyridine gave a diacetate, $C_{26}H_{36}O_7$ (III), in the IR spectrum of which there were the absorption bands of the carbonyl of an aliphatic acid (1710, 1740, and 1760 cm^{-1}), while at the same time, the absorption band of a hydroxy group was retained, i.e., the fertenidin molecule contains secondary and tertiary alcohol groups. The PMR spectrum of (III) confirmed the presence of a secondary hydroxyl, since in the spectrum of the diacetate (III) the signal of the gem-hydroxylic proton had undergone a paramagnetic shift ($\Delta\delta$ = 1.1 ppm). Furthermore, the signals of two acetyl groups appeared, at 2.0 ppm (alcoholic) and 2.25 ppm (phenolic). The signals of the methyls of an isopropyl group in the PMR spectrum of (III) had the form of two doublets (3 H each) at 0.75 and 0.80 ppm, with the same SSCC, J = 6 Hz.

The mass spectrum of fertenidin is similar to that of other esters of terpenoid alcohols [5, 7-11], having a characteristic peak with m/e 333 $(M - C_3H_7)^+$ corresponding to the fragment of the molecule without an isopropyl group, and also a peak at 238 $(M - C_7H_6O_3)^+$ [the residue of the sesquiterpene alcohol] and at 138 $(C_7H_6O_3)^+$ – the p-hydroxybenzoic acid molecule.

In view of the composition, the developed formula, and the presence of the $(M - 43)^+$ peak in the mass spectrum, and also the nature of the manifestation of the terminal methyls in the IR and PMR spectra and of the oxygen-containing functional groups, for the terpenoid moiety of fertenidin the most probable skeleton is that of the

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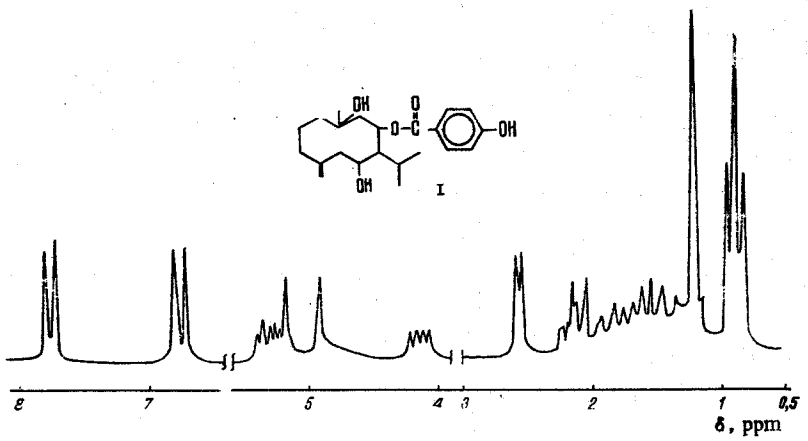

Fig. 1. PMR spectrum of fertenidin ($CDCl_3$).

sesquiterpene monocyclic hydrocarbon germacrane with an exomethylene group and a tertiary hydroxy group.

The chemical shift of the signal of the gem-hydroxylic proton (4.15 ppm) permits us to consider that it is present close to a double bond and is subject to its influence. On considering the multiplicities and the SSCCs of the signals of the methylene protons (d, J = 5 Hz) and of the gem-hydroxylic protons (q, J_1 = 10.5 Hz; J_2 = 5 Hz), in their interrelationship it can be seen that they are adjacent and undergo a vicinal interaction. Thus, the secondary hydroxy group is located at C_6.

On the basis of the multiplicity of the signal of the gem-acyl protons (m, $\Sigma_{1/2}$ = 22 Hz) only two positions remain for it: at C_2 or C_8.

It must be mentioned that in all the tens of sesquiterpene esters of the germacrane series isolated from plants of the genus Ferula [7-11], C_6 and C_8 have proved to be hydroxylated and acylated, this evidently being connected with features of the biogenesis of these substances in giant fennels and therefore structure (I) is the most likely for fertenidin.

Fertenicin (II) is an amorphous substance with the composition $C_{22}H_{30}O_4$, soluble in polar solvents and aqueous solutions of alkalis. The UV spectra of substances (I) and (II) each have an absorption maximum at 260 nm, which shows the presence of the same p-hydroxybenzoyl chromophore, but the values of log ε differ substantially (Δ log ε = 0.76). It is known that values of log ε > 4 apply to molecules with conjugated double bonds. Among esters, this phenomenon has also been observed in the UV spectra of ferocin [12] and juferin [13]. Consequently, the fertenicin molecule must also have conjugated double bonds. The IR spectrum (II) also contains the absorption bands of an aromatic nucleus (1520, 1590, 1615 cm^{-1}), of an ester carbonyl (1690 cm^{-1}), and of a hydroxy group (3200-3600 cm^{-1}).

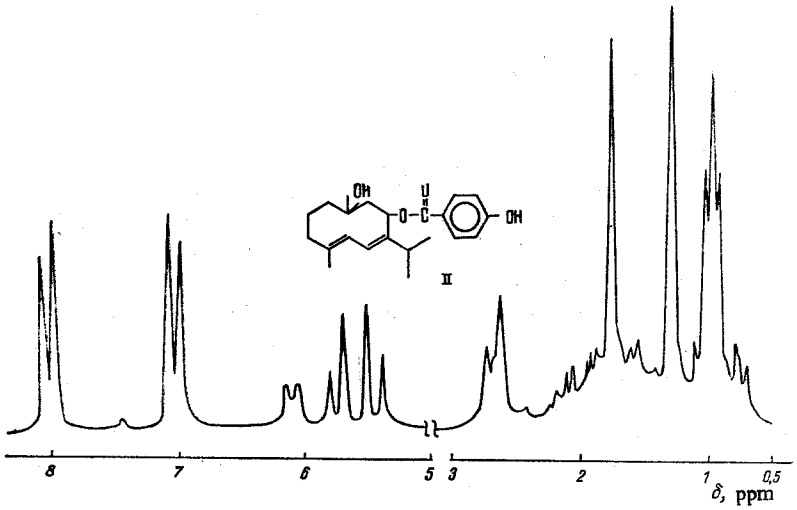

Fig. 2. PMR spectrum of fertenicin (C_5D_5N).

The nature of the signals in the PMR spectrum of (II) (deuteropyridine) is close to that for the PMR spectrum of (I): six-proton triplet at 0.94 ppm ($J_1 = J_2 = 7$ Hz), methyls of an isopropyl group; singlet at 1.25 ppm (3 H), methyl on a carbon atom attached to oxygen; singlet at 1.76 ppm (3 H), methyl on a double bond. In addition to this, the signals of two cis-olefinic protons appear at 5.45 and 5.76 ppm in the form of one-proton doublets with the same SSCC, J = 10 Hz. A multiplet at 6.15 ppm (1 H) must be ascribed to a gem-acyl proton. The paramagnetic shift of this signal into such a weak field may be due to the presence in the molecule of conjugated double bonds close to the gem-acyl proton and to a reduction of the electron density on it. In the weak-field region, as in the PMR spectrum of (I), are observed the signals of the protons of a p-hydroxybenzoic acid residue: doublets at 7.03 and 8.05 ppm with the same SSCC, J = 9.5 Hz.

The peaks of the ions in the mass spectrum of (II) with m/e 236 $(M - C_7H_6O_3)^+$ and 138 $(C_7H_6O_3)$ serve as a proof of the structural similarity of substances (I) and (II).

The spectral characteristics of fertenicin correspond to those of an ester of a germacrane alcohol having, as in fertenidin, a tertiary hydroxyl, an acyl residue (on the basis of the chemical shift and the multiplicity of the signal of the gem-acyl proton it may be assumed that it is located at C_8), and also two conjugated double bonds and a methyl group on a double bond.

In agreement with the facts given, structure (II) is suggested for fertenicin.

Fertenicin is probably a product of the dehydration of fertenidin in the plant.

EXPERIMENTAL

The conditions for recording the spectra have been given previously [5].

Separation and isolation were carried out by the method described previously [3]. From 20 g of resin containing the phenolic components of the roots of F. tenuisecta we obtained 0.11 g of fertenidin and 0.12 g of fertenicin.

Fertenidin (I), $C_{22}H_{32}O_5$, mp 236-238°C, $[\alpha]_D$ +145° (c 0.5; ethanol). Mass spectrum: 333 $(M-C_3H_7)^+$, 238 $(M - C_7H_6O_3)^+$, 220 $(M - C_7H_6O_3 - H_2O)^+$, 195 $(M - C_3H_7 - C_7H_6O_3)^+$, 138 $(C_7H_6O_3)^+$.

Fertenicin (II), $C_{22}H_{30}O_4$. Mass spectrum: 236 $(M - C_7H_6O_3)^+$, 218 $(M - C_7H_6O_3 - H_2O)^+$, 193 $(M - C_7H_6O_3 - C_3H_7)^+$, 175 $(M - C_7H_6O_3 - C_3H_7 - H_2O)^+$, 138 $(C_7H_6O_3)^+$, 121 $(C_7H_6O_3 - OH)^+$.

The acetylation of (I) was performed with acetic anhydride in pyridine, giving the diacetate $C_{26}H_{36}O_7$ with mp 108-110°C.

SUMMARY

Two new esters have been isolated from the roots of F. tenuisecta: fertenidin and fertenicin, and the structures of 6,10-dihydroxy-8-(p-hydroxybenzoyl)germacr-4(14)-ene and 10-hydroxy-8-(p-hydroxybenzoyl)germacra-4,6-diene, respectively, have been proposed as the most probable for them.

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