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STRUCTURE AND STEREOCHEMISTRY OF FERTIDIN

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The new ester, fertidin, has been isolated from the phenolic fraction of Ferula tenuisecta, and on the basis of chemical transformations and spectral characteristics its structure and stereochemistry have been established as 10α-angeloyloxy-4β-hydroxy-6α-p-hydroxybenzoyloxycarot-(9)-ene.

Continuing a study of the terpenoid compounds of plants of the genus Ferula (family Apiaceae), from the phenolic fraction of the total extractive substances of Ferula tenuisecta Korov by chromatographic separation on a column of KSK silica gel we have isolated a new ester with the composition $C_{27}H_{35}O_6$, mp 163-164°C (decomp.), which we have called fertidin (I).

A maximum at 260 nm (log ε 4.17) in the UV spectrum of fertidin showed the presence of a p-hydroxybenzoic acid residue in its molecule, while a bathochromic shift of the maximum ($\Delta\lambda_{max}$ = 40 nm) in an alkaline medium showed the presence of phenolic hydroxy group.

The IR spectrum of (I) contained strong absorption bands of two conjugated ester carbonyl groups (1690, 1715 cm^{-1}), of a double bond (1650 cm^{-1}), of an aromatic ring (1615, 1590, 1520 cm^{-1}), and of hydroxy groups (3250, 3450 cm^{-1}).

In the PMR spectrum of fertidin ($CDCl_3$) the strong-field region contained the signals of two secondary methyl groups —doublets at 0.8 and 0.9 ppm (3 H each, J = 7 Hz), of an angular methyl group — singlet at 1.16 ppm (3 H), and of a methyl at a double bond — broadened singlet at 1.74 ppm (3 H). In addition, the spectrum showed the signals of two gem-acyl protons — a sextet at 5.36 ppm (1 H, J = 11, 6, and 3 Hz) and a doublet at 4.83 ppm (1 H, J = 8 Hz). A doublet at 5.69 ppm (1 H, J = 8 Hz) related to an olefinic proton, and its components were broadened because of allyl interaction with a vicinal methyl group.

Two-proton doublets at 6.78 and 7.81 ppm (2 H each, J = 9.5 Hz) were due to the protons of the p-hydroxybenzoic acid residue, while a multiplet with its center at 6.01 ppm and a group of signals in the 1.8-1.95 ppm region were characteristic for the protons of an angelic acid residue.

A comparison of the facts given above with literature information on known esters isolated from plants of the genus Ferula [1-3] gave grounds for assuming that fertidin was an ester of a carotane sesquiterpene alcohol with angelic and p-hydroxybenzoic acids. In

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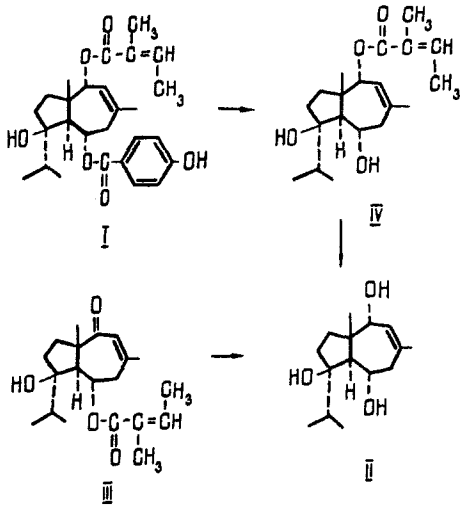
actual fact, the hydrolysis of the substance with a 5% aqueous solution of caustic soda led to the formation of two acids (angelic and p-hydroxybenzoic) and a sesquiterpene alcohol with the composition $C_{15}H_{26}O_3$ (II), mp 180-181°C, $[\alpha]_D$ + 42° (c 1.0; chloroform). From its physicochemical constants and IR spectrum, the latter was identical with pallinol, isolated on the alkaline hydrolysis of pallinin [4]. Pallinol had also been obtained previously by the reduction of lapidin (III) with sodium tetrahydroborate followed by hydrolysis [5].

The positions of the p-hydroxybenzoic and angelic acid residue in fertidin were determined in the following way: as mentioned above, the signals of the methyl groups of the isopropyl radical in the PMR spectrum of the substance were represented in the form of doublets at 0.8 and 0.9 ppm ($\Delta\delta$ = 0.1 ppm), which showed the position of the p-hydroxybenzoic acid residue at C_6 [6]. Hence, the angelic acid residue in fertidin was present at C_{10}.

The stepwise hydrolysis of fertidin with 5% sodium carbonate solution at room temperature gave pallinol angelate $C_{20}H_{32}O_4$ (IV), in the PMR spectrum of which the signal of the proton at C_6 had undergone a diamagnetic shift by 1.36 ppm in comparison with that of the initial compound.

On the basis of the facts given above, fertidin has the structure and relative configuration of 10α-angeloyloxy-4β-hydroxy-4β-hydroxy-6α-p-hydroxybenzoyloxycarot-8-ene.



EXPERIMENTAL

The conditions for taking the spectra have been described in [5].

Isolation of Fertidin. The residue after the separation of ferutin, ferutinin, and teferin [1] from the phenolic fraction of an ethanolic extract of the roots of Ferula tenuisecta (8.2 g) collected in Tashkent province was separated on a column of KSK silica gel (3 × 70 cm) with elution by hexane–ethyl acetate (4:1) and the collection of 20 ml fractions. Fractions 19-27 yielded 0.15 g of fertidin, $C_{27}H_{36}O_6$, mp 163-164°C (decomp.) (hexane–diethyl ether (1:1)).

Hydrolysis of Fertidin. a) A solution of 70 mg of fertidin in 20 ml of 5% sodium carbonate was left at room temperature overnight. Then the reaction mixture was diluted with water and was treated with diethyl ether (3 × 50 ml) and the ethereal extract was dried over sodium sulfate and the solvent was distilled off. This gave 0.09 g of pallinol monoangelate $C_{20}H_{32}O_4$. p-Hydroxybenzoic acid, $C_7H_6O_6$, with mp 210-212°C, was isolated from the acid fraction of the hydrolysate.

b) Pallinol monoangelate was hydrolyzed with a 5% aqueous alcoholic solution of caustic potash in the water bath for 2 h. From the hydrolysis products were isolated pallinol, $C_{15}H_{26}O_3$, mp 180-181°C, and angelic acid, $C_5H_8O_2$, mp 45-46°C.

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VAPOR-PHASE HYDROGENATION IN THE GLC ANALYSIS OF SESQUITERPENE LACTONES OF THE EUDESMANE SERIES

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The GLC analysis has been carried out of the products of the vapor-phase hydrogenation of the unsaturated lactoens of Inula helenium L. Tetrahydroalantolactone has been detected for the first time in elecampane rhizones and roots. During the vapor-phase hydrogenation of the compounds being analyzed in the presence of a Ni catalyst, a migration of the exocyclic double bond of isoalantolactone and of dihydroisoalantolactone was observed.

At the present time, the medical industry is producing the antiulcer drug Alanton, which consists of the total sesquiterpene lactones of the rhizomes and roots of elecampane, Inula helenium [1].

The GLC method has been proposed for the quantitative analysis of the active principles present in medicinal plant raw material and for the stagewise control of the Alanton production process [2, 3]. Six substances have been detected on a chromatogram of an elecampane extract [2].

In the GLC of authentic samples of sesquiterpene lactones isolated from elecampane rhizomes and roots [4] it was established that four of the peaks belonged to dihydroalantolactone (DA), alantolactone (A), dihydroisoalantolactone (DIN), and isoalantolactone (IA), their relative retention times (r) being 1.19, 1.34, 1.83, and 1.96, respectively (the standard substance being anthracene.

In the present paper we consider the identification of one more substance, with r = 1.62 detected on the chromatogram of elecampane rhizomes and roots.

In view of the fact that the elecampane sesquiterpenes have different degrees of saturation of the carbon-carbon bond in the eudesmane nucleus, we assumed the presence of the completely hydrogenated substance, i.e., natural tetrahydroalantolactone (TA). It has been known previously only as a product of the reduction of sesquiterpene compounds of the eudesmane series [5, 6].

With the aim of elucidating the possibility of the hydrogenation of these compounds during GLC, in place of helium we used hydrogen as the carrier gas. On comparing chromatograms of the elecampane extract obtained under identical conditions but with helium as the carrier gas in one case and hydrogen in the other, we detected a change in the ratio of the areas of the peaks of the substances under investigation. Table 1 shows the amounts of each compound in the total sequiterpene lactones calculated by the method of normalization with respect to the chromatogram obtaine don the use of helium as the carrier gas (Fig. 1a) and with respect to the chromatogram obtained on the use of hydrogen as the carrier gas (Fig. 1b).

It can be seen from Table 1 that on the use of hydrogen as the carrier gas the percentage of A present fell 6-fold while the percentages of DA and DIA in the mixture of sesquiterpene

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