THE STRUCTURE OF FEKORIN — A NEW ESTER FROM THE ROOTS OF Ferula korshinskyi

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From a methanolic extract of the roots of Ferula korshinskyi Eug. Kor. collected in the wooded slopes of the mountains in the environs of Lake Iskanderkul' (TadzhSSR), by chromatography on a column of silica gel we have isolated a substance with the composition $C_{22}H_{34}O_5$, bp 42°C/8 mm Hg, $[\alpha]_D^{23}$ −29° (c 0.94; chloroform), $[n]_D^{24}$ 1.491, R_f 0.8 (system 1), M^+ 378. The substance has a neutral character and is readily soluble in petroleum ether, diethyl ether, and chloroform, and insoluble in water.

In the UV spectrum of the substance there is a maximum with λ_{max} 222 nm (log ε 3.94) and in the IR spectrum absorption bands at 1745, 1720, and 1230–1270 cm^{-1} (ester carbonyl, carbonyl stretching vibrations), 1660 cm^{-1} (double bond), and 2880–2960 cm^{-1} (methyl and methylene groups). A consideration of the IR spectrum gave grounds for assuming that the substance was an ester. When it was hydrolyzed with a 5% solution of caustic potash, a sesquiterpene alcohol with the composition $C_{15}H_{26}O_3$, mp 82–83°C, $[\alpha]_D^{23}$ + 50° (c 1.5; ethanol) was obtained which was identified by its IR and NMR spectra and a mixed melting point and by its diacetate as ugamdiol, which we have isolated from Ugamian giant fennel [1, 2]. From the acid fraction of the hydrolyzate we isolated an acid with the composition $C_5H_8O_2$, mp 44–45°C, identical according to its IR spectrum with angelic acid, and by paper chromatography we detected acetic acid [3].

Thus, fekorin is a diester of ugamdiol and angelic and acetic acids. This is confirmed by the mass and NMR spectra of fekorin. In the mass spectrum of the substance there are peaks of ions with m/e 378 (M^+), 318 ($M - CH_3COOH$), and 279 ($M - C_5H_7O_2$). In the NMR spectrum of fekorin there are doublets at 0.95 and 1.10 ppm (J = 6 Hz, 3 H each), due to the methyl groups of an isopropyl radical, and singlets at 1.10 and 1.76 ppm (3 H each) assigned, respectively, to angular and vinyl methyl groups. Singlets at 1.8 ppm (3 H) and 1.9 ppm (3 H), and also doublets at 1.87 ppm (J = 3 Hz, 3 H) are due, respectively, to the methyl groups of acetyl and angeloyl residues. In addition, at 2.72 ppm there is a doublet from an epoxy proton (J = 6 Hz). The signals of geminal protons appear in the form of a doublet at 4.75 ppm (doublet, J = 6 Hz) and 5.3 ppm. On the latter is superposed the signal of an olefinic proton. The olefinic proton of angelic acid is observed in the form of a quartet with secondary splitting at 5.96 ppm. There are two hydroxy groups in the ugamdiol molecule — at C_6 and C_8.

In order to establish the structure of fekorin it was necessary to determine the position of each of the acid residues. In the stereochemical respect, the acyl residue in the C_8 position is probably in a more

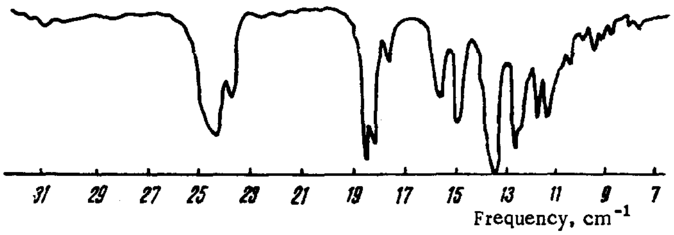

Fig. 1. IR spectrum of fekorin.

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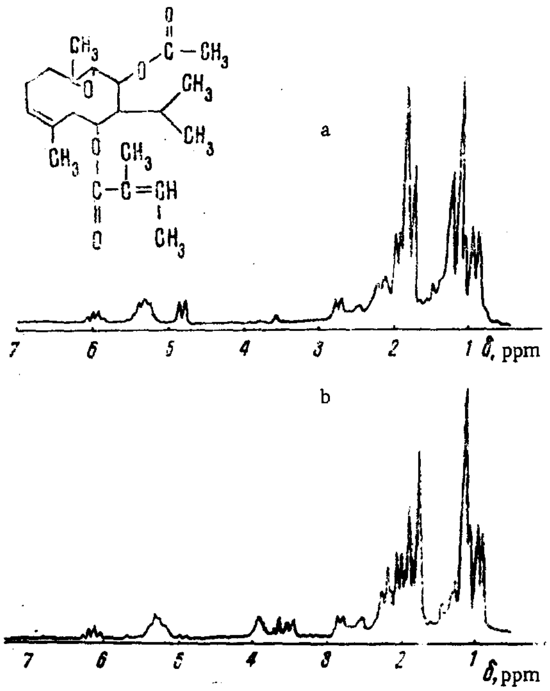

Fig. 2. NMR spectrum of fekorin (a) and the monoester (b).

favorable position energetically then the same grouping at C_8. Consequently, the acyl residue at C_8 should be more labile and, on hydrolysis, be split off first. In actual fact, mild acid hydrolysis of fekorin with 1% methanolic caustic potash in the cold led to the formation of a monoester and acetic acid. In the IR spectrum of the monoester, the absorption band of one of the carbonyls (1745 cm^{-1}) had disappeared, and the absorption band of a hydroxy group (3200-3600 cm^{-1}) had appeared. In the NMR spectrum of the monoester, the signal of one of the geminal protons, namely the doublet at 4.75 ppm corresponding to H-8, had shifted to 3.5 ppm and, simultaneously, the singlet signal at 1.8 ppm due to the acetyl group had disappeared. These facts show that in the diester the acetic acid residue is present in the C-8 position and the angelic acid residue at C-6. On saponification under severe conditions, the second acyl residue was also split off, as was shown by the disappearance of the signals of the protons of the angelic acid residue and by the displacement of the quartet corresponding to H-6 from 5.30 to 4.14 ppm. On the basis of the facts given above, it may be concluded that fekorin has the structure of 8-acetoxy-6-angeloyloxy-9,10-epoxygermacr-3-ene.

EXPERIMENTAL METHOD

The UV spectra were taken on a Hitachi instrument, the IR spectra on a UR-10 spectrometer (in KBr), and the NMR spectra on a JNM-4H-100/100 MHz instrument in $CDCl_3$, the chemical shifts being given in the δ scale from the signal of HMDS taken as 0. TLC was performed in a fixed layer of KSK silica gel in the following systems: 1) petroleum ether–ethyl acetate (3 : 1); 2) butan-1-ol saturated with 1.5 N ammonia. The esters were revealed with a 1% solution of vanillin in concentrated sulfuric acid, and the acids with a 0.04% ethanolic solution of Bromophenol Blue.

Isolation of Fekorin

The comminuted roots of Ferula korshinskyi were steeped three times with methanol (60, 45, and 40 liters). The combined methanolic extracts were concentrated to three liters, diluted with water (2 : 1), and treated with ether (5 × 1 liter). After elimination of the solvent, 290 g of viscous extract was obtained.

The combined extractive substances (10 g) were deposited on a column (h 50, d 5 cm) filled with KSK silica gel and eluted with a mixture of petroleum ether and ethyl acetate (3 : 1), 50-ml fractions being collected.

Fractions 9-18, after the distillation of the solvent, yielded 2.1 g of an oily substance with Rf 0.8 (system 1), composition $C_{22}H_{34}O_5$ (mol. wt. 378, mass spectrometrically), $[\alpha]^{21}_{D}$ −29° (c 0.94; chloroform).

Severe Hydrolysis of Fekorin

Production of Ugamdiol. A solution of 0.3 g of the substance in 30 ml of a 3% solution of caustic potash in methanol was heated for two hours. The solvent was distilled off in vacuum, the residue was diluted with water, and the neutral fraction was extracted with ether. The ethereal extract was washed with water, dried, and distilled. The residue was crystallized from petroleum ether in the form of colorless needles with mp 82-83°C, $[\alpha]_D^{23} = +50°$ (c 1.5; ethanol).

Isolation of Angelic Acid. The residue after the extraction of the ugamdiol was acidified with 5% HCl, and the acid part was extracted with ether. On chromatography in system 2, the ethereal extract gave two spots with R_f 0.13 and 0.45 corresponding to acetic and angelic acids. When the ethereal extract was concentrated, crystals deposited with mp 44-45°C which were identified by their IR spectrum as angelic acid [4].

Mild Hydrolysis of Fekorin

Formation of a Monoester. A solution of 0.15 g of fekorin in 30 ml of 1% methanolic caustic potash was left at room temperature for 1.5 h. Then the liquid was diluted with water and extracted with ether. After the ether had been distilled off, a monoester with R_f 0.6 was obtained. The mother solution was acidified with 5% HCl, and on treatment with ether an acid fraction was isolated which was investigated by paper chromatography. In system 2 a spot with R_f 0.13 was obtained, which corresponds to acetic acid.

Ugamdiol Diacetate

The alcohol (0.1 g) was acetylated with acetic anhydride (3 ml) in pyridine (3 ml) with heating for four hours. The reaction product was isolated in the usual way, giving colorless crystals with mp 110-111°C (from ether).

SUMMARY

From the roots of Ferula korshinskyi Eug. Kor. we have isolated a new ester with the composition $C_{22}H_{34}O_5$, $[\alpha]_D^{23} - 29°$ (c 0.94; chloroform) n_D^{24} 1.491, bp 42°C/8 mm Hg, which we have called fekorin. On the basis of a study of the products of hydrolysis and also spectral characteristics, it has been established that fekorin is 8-acetoxy-6-angeloyloxy-9,10-epoxygermacr-3-ene.

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