THE STRUCTURES OF CHIMGANIN AND CHIMGIN

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As is well-known, numerous species of the genus Ferula are distinguished by the great diversity of the components which they contain. For example, in F. badrakema K. Pol., F. gummosa Boiss, F. samarkandica Eug. Kor. coumarins consisting of ethers of umbelliferone and sesquiterpene alcohols, and in F. oopoda Boiss and F. badhysii Eug. Kor. sesquiterpene lactones of the azulene series or terpenoid diols (ugamdiol, chimgandiol, angrendiol, ovindiol [1, 2]) have been found. The simultaneous presence of coumarins and sesquiterpene lactones in representatives of this genus has not been observed.

Central Asian species of Ferula of the section Xeronarthex are known as sources of a large group of terpenoids.

On studying the roots of F. tschimganica Lipsky which we collected during the period of the incipient formation of fruit (June 1971) on the slopes of the Great Chimgan at a height of 1900 m above sea level, we found in it two aromatic compounds with R_f 0.94 (1) and 0.66 (3) which gave an orange coloration with diazotized sulfanilamide. We separated these components by chromatography and obtained two new substances, which we have called chimganin and chimgin.

Chimganin has the composition $C_{18}H_{24}O$, mp 85°C (petroleum ether), $[\alpha]_D^{24}$ +5° (c 0.96; ethanol) and forms colorless crystals readily soluble in benzene, ethanol, and ether, and insoluble in water.

On being heated in the presence of sodium carbonate, they dissolve in water and on subsequent acidification they separate from solution in unchanged form. Chimganin does not give a reaction with ferric chloride, but forms colored products with diazotized sulfanilamide. In spite of these properties, somewhat imitating coumarins, it is not a coumarin, as is shown by its UV spectrum.

The UV spectrum has maxima at 265 and 295 nm (log ε 3.49, 3.34) and a minimum at 284 nm (log ε 3.36), which are characteristic for a benzene ring substituted by two oxygen atoms. The IR spectrum (Fig. 1a) shows a broad band at 3300-3500 cm^{-1} (hydroxyl) and other bands at (cm^{-1}) 1610, 1525, 1470 (aromatic nucleus), 900, 840 (1,2,4-substituted benzene ring), 1695, 1230, 1320, 1115 (ester of an unsaturated acid), and 1170, 1370 (gem-dimethyl group).

In its NMR spectrum (Fig. 2), one-proton doublets at 7.48 and 6.78 ppm, J = 8 Hz, are due to ortho-interacting protons in an aromatic nucleus. A broadened singlet at 7.44 ppm (1 H), superposed on one of the components of the first doublet, is due to protons in the meta position. A paramagnetic shift of the signals of the first and third protons relative to the chemical shift of the protons of the unsubstituted benzene ring, amounting to +0.21 and 0.17 ppm, respectively, is caused by the carbonyl group of an ester located in the ortho position. The diamagnetic shift of the signal of the second proton (Δ −0.45 ppm) is due to the donor influence of a hydroxy or methoxy group. The presence of one methoxy group and its position in the aromatic nucleus are confirmed by a three-proton singlet at 3.80 ppm, and that of a hydroxy group by a broad signal in the 6.5 ppm region disappearing on deuterium exchange. The presence of a phenolic hydroxyl is shown by a 52-nm bathochromic shift of the long-wave maximum in the UV spectrum in the presence of caustic alkali.

The facts presented permit the conclusion that the aromatic moiety of chimganin is based on the residue of 3-hydroxy-4-methoxy- or 4-hydroxy-3-methoxybenzoic acid, which is confirmed by the presence in the mass spectrum of fragments with m/e 168 and 151, corresponding to the aromatic and terpenoid parts of the molecule.

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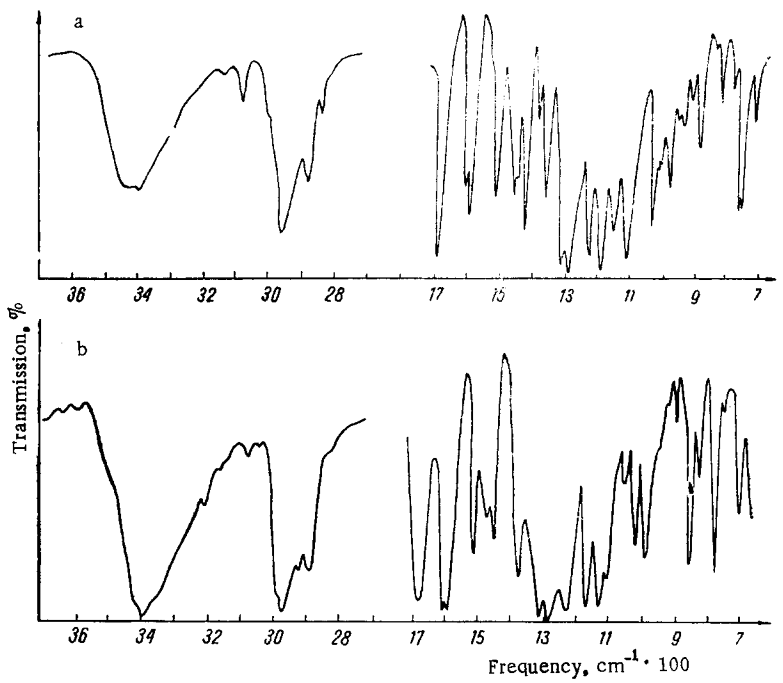

Fig. 1. IR spectra (KBr) of chimganin (a) and chimgin (b).

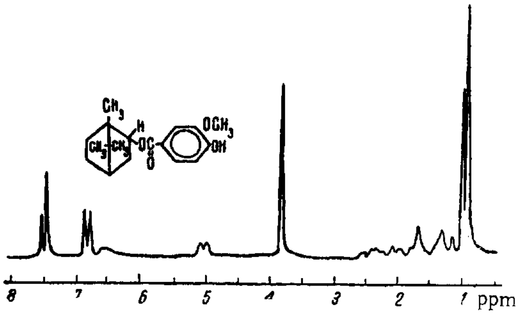

Fig. 2. NMR spectrum of chimganin (CCl_4).

Thus, chimganin is an ester of an aromatic acid with the composition $C_8H_8O_4$ and a terpenoid alcohol $C_{10}H_{18}O$. The latter contains two methyl groups present on a quaternary carbon atom, and one methyl group attached to a tertiary carbon atom, as is shown by the presence in the NMR spectrum of a six-proton singlet at 0.84 ppm and a doublet at 0.88 ppm, J = 6 Hz (3 H). A doublet at 4.99 ppm, J = 10 Hz (1 H), with traces of secondary splitting (half-width of the component about 5 Hz) can be ascribed to a methine proton on a carbon atom connected with an ester grouping. With the given composition and in the absence of double bonds, the terpenoid moiety of chimganin can have only a bicyclic structure, and therefore the signals in the 1.2 ppm with an intensity of 7 H most probably correspond to equatorial and axial protons.

We subjected chimganin to alkaline hydrolysis, which gave an acid with mp 205-206°C and a hydroxy terpene with mp 197°C, $[\alpha]_D^{24}$ +10° (c 1.0; ethanol) with a camphor-like odor.

The acid was identified by its composition, melting point, the formation of an acetate with mp 138-140°C, and qualitative reactions as vanillic acid (literature data: mp of the acid 207°C and of its acetate 142°C), and the hydroxy terpene was similarly identified as (+)-borneol (literature data: mp 206.5°C). Since the splitting constant of the methine proton is high (J = 10 Hz), it may be concluded that the latter is in the axial position and the acyloxy group is in the equatorial position.

Chimgin has the composition $C_{17}H_{22}O_3$, mp 155°C (petroleum ether), $[\alpha]_D^{24}$ +4.9° (c 1.02; ethanol), and has properties (solubility in organic solvents, behavior with alkalis, and color reactions) similar to those of chimganin.

Its UV spectrum has only one maximum: λ_{max} 260 nm (log ε 5.28), which undergoes a 42-nm bathochromic shift in the presence of alkali, these facts showing that it contains a benzene ring and a phenolic hydroxyl.

The IR spectrum of chimgin (Fig. 1b) shows absorption bands at (cm^{-1}) 3350-3450 (hydroxyl), 1610, 1520, 1475 (aromatic nucleus), 825 (1,4-disubstituted benzene ring), 1690, 1240, 1320, 1110 (unsaturated ester), and 1175, 1380 (gem-dimethyl group). The NMR spectrum (Fig. 2) shows two two-proton doublets at 7.84 and 6.82 ppm, J = 8 Hz), corresponding to two pairs of aromatic protons in the ortho positions. The signals of two protons are shifted downfield with Δ +0.57 ppm and two signals are shifted upfield with Δ −0.45 ppm, which is caused by the factors noted in the case of chimganin.

A broadened signal in the 8.15 ppm region which disappears on deuterium exchange, is due to a phenolic hydroxyl (see also the bathochromic shift of the UV maximum on the addition of alkali). All the other signals in the NMR spectrum, corresponding to the terpenoid part of the molecule, are completely identical with those for chimganin.

The facts presented show that the aromatic part of the chimgin molecule is 4-hydroxybenzoic acid, and the terpenoid part is the above-mentioned (+)-borneol.

In actual fact, alkaline hydrolysis of the substance gave an acid with mp 209-210°C (forming an acetate with mp 207-209°C), identified by p-hydroxybenzoic acid, and a hydroxyterpene with mp 197°C identical by its IR spectrum and by a mixed melting point with the (+)-borneol isolated in the hydrolysis of chimganin. Thus, chimgin is the ester of p-hydroxybenzoic acid and (+)-borneol.

The components that we have isolated are apparently representatives of a broad group of compounds in which sesquiterpenes are bound with aromatic acids in the form of esters.

EXPERIMENTAL

The NMR spectra were taken on a JNM-4H-100/100 instrument (CCl_4), the chemical shifts being given in the δ scale from the signal of HMDS taken as 0; the IR spectrum was taken on a UR-10 spectrometer (KBr); and the UV spectra were recorded on a Hitachi spectrometer. Thin-layer chromatography (TLC) was performed in a fixed layer of KSK silica gel with benzene−methanol (95 : 5) as the mobile phase.

Isolation of Chimganin. The dried comminuted roots (1.4 kg) were treated with 8 liters of methanol for 24 h, the operation being repeated three times. The extract was concentrated to 3 liters, diluted with water (2 : 1), and extracted with diethyl ether (3 × 0.5 liter). This gave 2.3 kg of a viscous extract, 30 g of which was deposited on a chromatographic column filled with KSK silica gel (height 18 cm, diameter 9 cm). The column was washed with 25 liters of petroleum ether. When the eluate was concentrated, 8 g of an oily residue deposited which was washed with cooled petroleum ether and recrystallized from the same solvent. This gave 3 g (1.5% of the initial raw material) of a colorless crystalline substance with the composition $C_{18}H_{24}O_4$, mp 85°C (from petroleum ether).

Saponification of Chimganin. A. Isolation of Borneol. A mixture of 2.5 g of the substance and 50 ml of 5% caustic potash solution was heated in the water bath under reflux. The liquid (A) was cooled and treated with ether (3 × 50 ml), and the extract was distilled. The residue was recrystallized from petroleum ether and was then sublimed in vacuum. The sublimate consisted of a crystalline substance with mp 197°C.

B. Isolation of 4-Hydroxy-3-methoxybenzoic Acid. The liquid A was acidified and treated with ether (3 × 50 ml). The extract was distilled and the residue was crystallized from petroleum ether and was then sublimed in vacuum. This gave a crystalline substance with mp 205-206°C. The acetate of 4-hydroxy-3-methoxybenzoic acid was obtained by heating the substance with acetic anhydride for 2 h in the usual way. Mp 138-140°C (from methanol).

Isolation of Chimgin. After the elution of the chimganin, the chromatographic column was washed with 3 liters of a mixture of petroleum ether and benzene (4 : 5). The eluate was distilled, and the residue (6 g) was crystallized from petroleum ether. This gave 2.5 g (1.25% of the initial raw material) of a crystalline substance $C_{12}H_{22}O_3$, mp 154-155°C.

The saponification of the chimgin and the isolation of (+)-borneol and of 4-hydroxybenzoic acid were performed by the methods described for chimganin. We obtained (+)-borneol with mp 197°C, 4 hydroxybenzoic acid with mp 209-210°C, and the acetate of the latter with mp 207-209°C.

SUMMARY

The roots of Ferula tschimganica Lipsky have yielded two new compounds with the compositions $C_{18}H_{24}O_4$ (mp 85°C) and $C_{17}H_{22}O_3$ (mp 155°C), which have been called chimganin and chimgin. On the basis of their UV, IR, and NMR spectra and the products of alkaline hydrolysis, it has been shown that chimganin is the ester of 4-hydroxy-3-methoxybenzoic acid and chimgin that of 4-hydroxybenzoic acid with (+)-borneol.

LITERATURE CITED

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