THE STRUCTURE OF ALATOL

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Osthole, isoimperatorin, oxypeucedanin, oxypeucedanin hydrate, marmezin, and a new furocoumarin (I), $C_{17}H_{18}O_6$, with mp 125-127°C, which we have called alatol, have been isolated from a chloroform extract of the roots of Prangos alata Grossh. (Prangos biebersteinii Karjag). The present paper gives the results of a study of the structure of (I).

The IR spectrum of (I) (Fig. 1a) shows characteristic absorption bands at (cm^{-1}) 3370 (OH), 1710 (C =O of an α-pyrone ring), 1615, 1600, 1570, and 1540 (aromatic nucleus), and 1350 (gem-dimethyl grouping). From the nature of the splitting of the absorption bands in the 1550-1630 cm^{-1}, the IR spectrum of (I) is very similar to the spectra of 5-monosubstituted furocoumarins, especially gosferol, pranferol, and oxypeucedanin hydrate, which shows that (I) belongs to this group of compounds.

The presence of a hydroxy group in the molecule of (I) was confirmed by the preparation of a monoacetyl derivative (II), $C_{19}H_{20}O_7$, mp 109-110°C, the IR spectrum of which lacked the absorption band of an OH group.

The oxidation of (I) with chromium trioxide in glacial acetic acid formed a ketone (III), $C_{17}H_{16}O_6$, mp 154-156°C, which shows the presence in the molecule of (I) of a secondary hydroxy group, and a compound (IV), $C_{13}H_8O_6$, mp 265-266°C, identified as oxypeucedaninic acid, which shows the presence in (I) of a side chain attached to the aromatic nucleus through a $-O-CH_2-$ group in position 5. Substance (IV) was also formed by the oxidation of (II) under similar conditions.

In the NMR spectrum of (I) (Fig. 2a), in the strongest field there is a signal from two methyl groups at δ 1.23 ppm with an intensity of six proton units. This signal must be ascribed to the protons in a gem-dimethyl grouping. A broadened singlet at δ 2.85 ppm with an intensity of one proton unit may be ascribed to the proton of the hydroxy grouping. A signal at δ 3.28 ppm with an intensity of three proton units is due to the protons of the methoxy group. A multiplet in the δ 4.20-4.70 ppm region with an intensity of three proton units relates to the protons of a $-\underset{|}{C}H-CH_2-O-Ar$ group. In a weaker field are found doublets with chemical shifts of δ 6.32, 8.35 ppm (J = 10 Hz) and 7.08, 7.65 ppm (J = 2 Hz) due to the 3,4-protons of the coumarin ring and the 4',5'-protons of the furan ring, respectively. A singlet at δ 7.20 ppm is due to the proton in position 8.

The NMR spectrum of (II) (Fig. 2b) shows an additional singlet at δ 2.05 ppm (3H) due to the protons of the methyl group of an acetyl radical. As was to be expected, the signal from the methine proton adjacent to the methylene group has undergone a paramagnetic shift and appears in the form of a multiplet at δ 5.40 ppm.

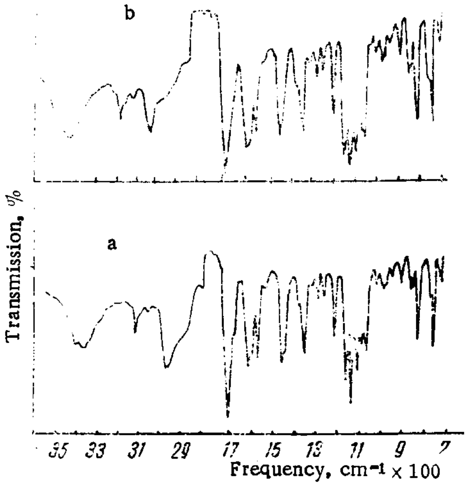

Fig. 1. IR spectra of natural (a) and synthetic (b) alatol.

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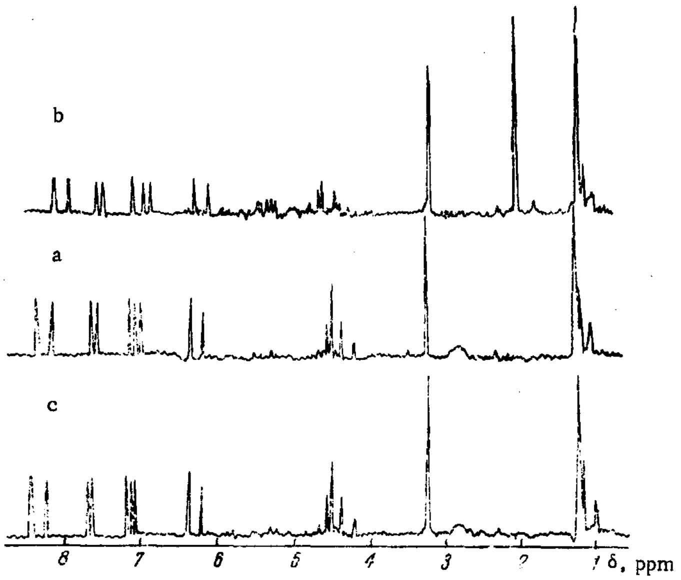


Fig. 2. NMR spectra of natural alatol (a) of the acetate of natural alatol (b), and of the acetate of synthetic alatol (c).

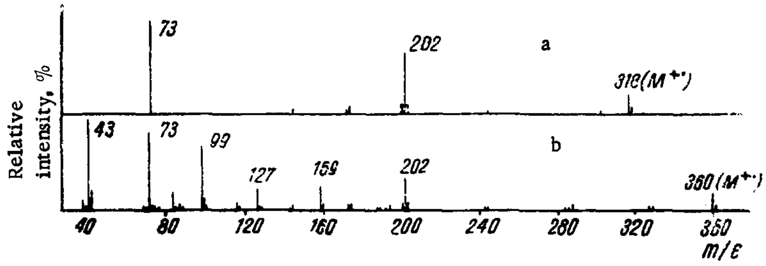
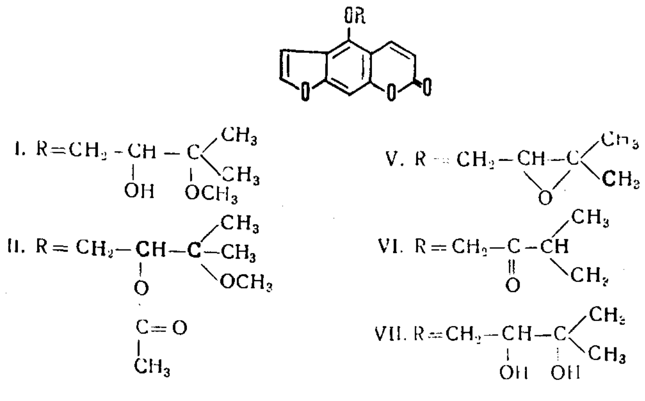


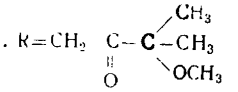
Fig. 3. Mass spectra of alatol (a) and of the acetate of natural alatol (b).

From what has been said it follows that compound (I) has the structure of 5-(2"-hydroxy-3"-methoxy-3"-methylbutoxy)-furo-2',3':7,6-coumarin.

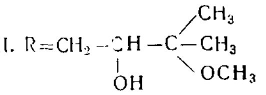
The structure of (I) was confirmed by partial synthesis and by mass spectra. When natural oxypeucedanin (V), $C_{16}H_{14}O_5$, was treated with 20% sulfuric acid in methanol, in addition to isooxypeucedanin (VI), $C_{16}H_{14}O_5$, mp 145-146°C, and oxypeucedanin hydrate (VII), $C_{16}H_{16}O_6$, mp 133°C, the reaction mixture yielded a substance (VIII), $C_{17}H_{18}O_6$, mp 126.5-128.5°C, identical with (I) according to mixed melting points with authentic samples and IR and PMR spectra (Fig. 1b: Fig. 2c, respectively). It has been reported previously [2] that under these conditions the alkoxylation of the tertiary hydroxy group in the side chain of (VII) formed by the hydration of (V) takes place, which also leads to (VIII).

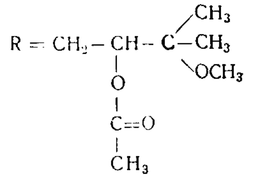
The acetylation of (VIII) with acetic anhydride in pyridine gave a monoacetyl derivative (IX), $C_{19}H_{20}O_7$, mp 108-110°C, identical with (II).



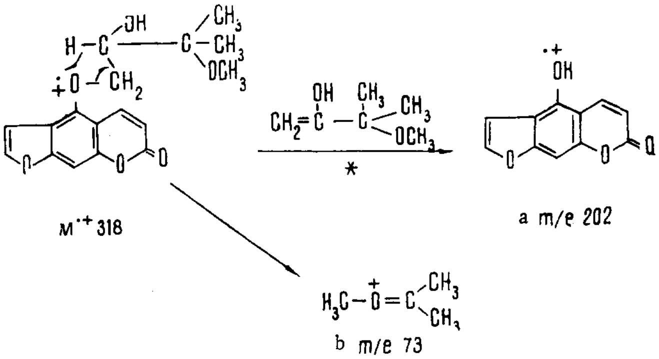
III.

$R=CH_2-\underset{\overset{\|}{O}}{C}-\overset{CH_3}{\underset{OCH_3}{C}}-CH_3$

IV. R=CH$_2$–COOH

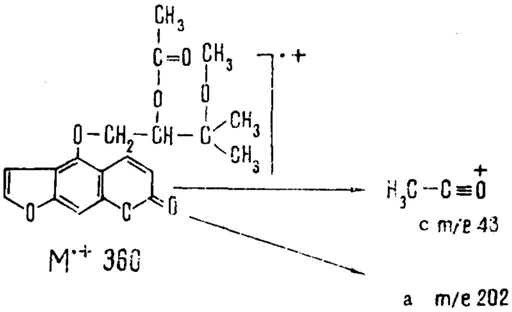
VIII.

$R=CH_2-\underset{\overset{|}{OH}}{CH}-\overset{CH_3}{\underset{OCH_3}{C}}-CH_3$

IX.

$R=CH_2-\underset{\overset{|}{O-\underset{CH_3}{C}=O}}{CH}-\overset{CH_3}{\underset{OCH_3}{C}}-CH_3$

The results of a study of the mass spectra of (I) and (II) (Fig. 3a,b, respectively) show that the main direction of fragmentation of these compounds is the formation of the ion *a* with m/e 202, which is connected with the migration of the hydrogen atom to the charged oxygen [2, 3]. The ion with m/e 73, forming the maximum peak in the spectrum, evidently corresponds to the structure b.



The fragmentation of (II) is basically similar to that of (I). The presence of an acetyl group in (II) leads to the formation of an ion c with m/e 43. The peaks of ions with m/e 99, 127, and 159 are also due to the acetyl group [3].



EXPERIMENTAL

The NMR spectra were taken on a JNM-C-60HL spectrometer (deuterated chloroform, internal standard HMDS), the mass spectra on an MKh-1303 instrument, and the IR spectra on a UR-20 spectrometer (paraffin oil). The melting points were determined on a Kofler block. Thin-layer chromatography was performed on a nonfixed layer of alumina (activity grade IV) using ethyl acetate–benzene (1 : 4) as the mobile phase. The analyses of all the compounds corresponded to the calculated figures.

Isolation of Alatol (I). The air-dry roots (500.0 g) were extracted with chloroform (3 × 2 liters). The chloroform was distilled off under vacuum, and the resulting residue (45.0 g) was chromatographed on a column of alumina (300.0 g; activity grade III) using as solvents benzene, benzene–chloroform (1 : 2 and 1 : 1), and chloroform. After the elimination of the solvent by distillation, the chloroform fractions yielded a crystalline substance (I), $C_{17}H_{18}O_6$, mp 125-127°C (from benzene), R_f 0.41. Yield 0.75 g.

Acetylation of (I). A mixture of 0.050 g of (I) with 2 ml of acetic anhydride and 0.5 ml of pyridine was heated for 5 h. Then it was diluted with water and worked up in the usual way, to give 0.035 g of the acetyl derivative (II), $C_{19}H_{20}O_7$, mp 109-111°C (ether), R_f 0.64.

Oxidation of (I). A solution of 0.0504 g of (I) in 1 ml of glacial acetic acid was treated with 0.2 g of chromium trioxide in 5 ml of 50% acetic acid, and the mixture was left at room temperature for a day. Two substances were isolated from the reaction products: (III), $C_{17}H_{16}O_6$, mp 154-156°C (ether), R_f 0.69, and (IV), $C_{13}H_8O_6$, mp 265-266°C (ethanol), identical with oxypeucedaninic acid. The main product of the reaction was (III) (yield 0.03 g).

Oxidation of (11). The oxidation of 0.1 g of (II) was performed under the conditions described above. This gave only oxypeucedaninic acid (IV) with mp 264-266°C (ethanol). Yield about 0.062 g.

Partial Synthesis of (I). A solution of 1.0 g of natural oxypeucedanin (V) in 25 ml of methanol was treated with 30 ml of 20% H_2SO_4 and the mixture was heated in the water bath for 5 h. From the reaction products, in addition to isooxypeucedanin (VI), $C_{16}H_{14}O_5$, mp 145-146°C (ethanol), R_f 0.77, and oxypeucedanin hydrate (VII), $C_{16}H_{16}O_6$, mp 133°C (benzene), R_f 0.06, was isolated 0.47 g of substance (VIII), $C_{17}H_{18}O_6$, mp 126.5-128.5°C (benzene), identical with alatol (I).

Acetylation of (VIII). Compound (VIII) (0.075 g) was acetylated by the usual method (see [1]). This gave 0.087 g of the monoacetyl derivative (IX), $C_{19}H_{20}O_7$, mp 108-110°C (ether), identical with (II).

SUMMARY

From the roots of Prangos alata Grossh (Prangos biebersteinii Karjag) a new furocoumarin (I), $C_{17}H_{18}O_6$, mp 125-127°C (from benzene), which has been called alatol, has been isolated.

On the basis of the results of IR and NMR spectra and chemical properties, the structure of 5-(2"-hydroxy-3"-methoxy-3"-methylbutoxy)-furo-2',3':7,6-coumarin has been proposed for (I). This structure has been confirmed by the partial synthesis and by the mass spectra of alatol and of its acetate.

LITERATURE CITED

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3. A. Z. Abyshev, P. P. Denisenko, N. P. Kostyuchenko, A. I. Ermakov, and Yu. N. Sheinker, Khim. Prirodn. Soedin., 49 (1972).