COUMARINS OF THE ROOTS OF *Heracleum leskovii*

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In the present paper we describe the isolation and chemical study of the coumarins of the roots of *Heracleum leskovii* Grossh. (Leskov's cow parsnip). The plant was grown by I. F. Satsyperova at the scientific-experimental station of the V. L. Komarov Botanical Institute of the Academy of Sciences of the USSR at Otradnoe.

After the extraction of the coumarins from the cow parsnip roots followed by separation on columns of acidic alumina, 13 substances were obtained (see Experimental part), including heracol, which has previously been isolated from *Heracleum antasiaticum* Manden [1], 6-isopentenyloxy-5-methoxyangelicin is known for *Angelica genuflexa* Nutt. [2], this being the first time it has been isolated from the genus *Heracleum*, and heraclesol — a new furocoumarin of the angelicin series.

Heraclesol (I in the Scheme of transformations) was revealed on a chromatogram in the form of a brown spot similar to 5,6- or 5,8-substituted derivatives of angelicin and psoralen, respectively.

The UV spectrum exhibited a number of maxima [λ_{max} (in ethanol) 223, 254, 306 nm (log ε 4.58, 4.64, 4.28)] characteristic for angelicin derivatives with maxima close to those of pimpinellin [3]. The IR region of the spectrum showed the bands of alcoholic OH groups at 3525 and 3400 cm^{-1}, the CH of a furan ring (3170 cm^{-1}), asymmetric and symmetric stretching vibrations of CH_3 groups (2980, 2950, 2860 cm^{-1}), the C=O of an α-pyrone ring (1715 cm^{-1}), and bands characteristic for C=C bonds of furocoumarins (1624 and 1577 cm^{-1}). The elementary composition was similar to that of biacangelicin [2].

The substance investigated was hydrolyzed to a phenolic compound (II), which, on methylation, was converted into 5,6-dimethoxyangelicin (pimpinellin — III).

On the basis of the difference in molecular weight and elementary compositions of the initial substance (I) and the products of hydrolysis (II) it was possible to assume the presence in the molecule of (I) of a $-OCH_2-CHOH-C(CH_3)_2OH$ radical. This hypothesis was confirmed by the PMR spectrum, which contains the following signals (δ, ppm): 1.27 and 1.30 (6 H, s, two methyl groups), 3.22 (2 H, broadened s, 2 OH groups), 3.81 (1 H, q, X proton of an ABX system, J_{AX} = 3.5 Hz, J_{BX} = 7.5 Hz), 4.25 (1 H, q, B proton of the ABX system, J_{BX} = 7.5 Hz, J_{AB} = 9.5 Hz), and 4.55 (1 H, q, A proton of the ABX system, J_{AX} = 3.5 Hz, J_{AB} = 9.5 Hz). The PMR spectrum contains a signal at 4.02 ppm (3 H, OCH_3 group).

Heraclesol (I) forms an acetonide (III), which shows the presence of a cis-glycol grouping in its molecule. In the PMR spectrum of the acetonide the signal at 3.22 ppm has disappeared and the signals of methyl groups have appeared (1.18, 1.34, and 1.37 ppm, 12 H, four methyl groups).

The results obtained give grounds for asserting the presence of an angelicin nucleus substituted in the 5' and 6' positions by CH_3O and $-OCH_2-CHOH-C(CH_3)_2OH$.

The position of attachment to the angelicin nucleus of the $-OCH_3$ and $-OCH_2-CHOH-C(CH_3)_2OH$ groups was established by comparing the physicochemical properties of the hydrolysis product (II) with those of 6-hydroxy-5-methoxyangelicin [2].

The hydrolysis product (II) gave no depression of the melting point in admixture with 6-hydroxy-5-methoxyangelicin, which was obtained from 6-isopentenyloxy-5-methoxyangelicin (V).

The shape of the optical rotatory dispersion curve of heraclesol is similar to that of biacangelicin [6], which gives grounds for assigning the R configuration to the asymmetric center at C-2.

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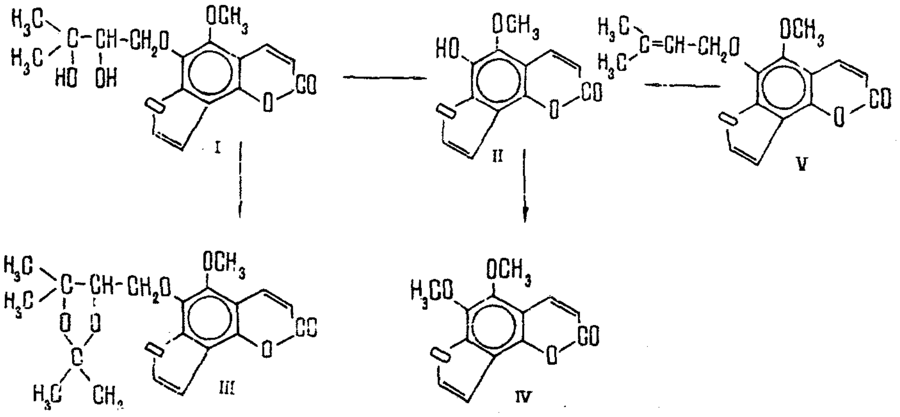

Chemical transformations of heraclesol

Thus, the structure of heraclesol can be represented as (+)-6-[2(R), 3-dihydroxy-3-dimethylbutoxy]-5-methoxyfuro-2',3':7,8-coumarin.

EXPERIMENTAL

For column chromatography we used acidic alumina [4]. The IR spectra were recorded on an IR-27G spectrophotometer in a tablet of KBr (1 mg of the substance under investigation in 200 mg of KBr), and the PMR spectra on a R-12A instrument (60 MHz) in $CDCl_3$ solutions (for heraclesol) and CCl_4 solutions (for heraclesol acetonide) with tetramethylsilane as internal standard. The melting points were determined on a Kofler block. The analyses of all the compounds corresponded to the calculated figures.

Isolation of the Coumarins. The coumarins were extracted from 1.5 kg of comminuted air-dry roots of Leskov's cow parsnip with 7.5 liters of acetone. The extract obtained was evaporated until the solvent had been completely eliminated. The viscous residue was dissolved in 100 ml of chloroform and passed through a column of acid alumina (5 × 8 cm), after which the column was washed with 150 ml of chloroform. The extract purified in this way was evaporated to 70 ml, mixed with 50 g of acidic alumina, dried, and deposited on a column of alumina (70 × 3.5 cm). Elution was performed initially with petroleum ether. The first fractions contained fats and osthole. Then the other coumarins were separated by the method described previously [4, 5], using diethyl ether as eluent. The fractions containing a mixture of coumarins were reseparated similarly. As a result we obtained the following substances in the individual crystalline state: psoralen (9 mg), bergapten (102 mg), xanthotoxin (11 mg), isopimpinellin (10 mg), phellopterin (8 mg), angelicin (18 mg), sphondin (98 mg), isobergapten (87 mg), and 6-ispentenyloxy-5-methoxyangelicin (25 mg, mp 95-96°C).

After the elution of the coumarins mentioned above with diethyl ether, three yellow zones remained on the column; these were cut out, and the substances were desorbed from the alumina with chloroform. The solvent was evaporated off and the residues were crystallized from ethanol. The following substances were isolated: biacangelicin (1500 mg), heraclesol (95 mg), and heracol (13 mg, mp 148-151°C, $[\alpha]_D^{20}$ +18°, absolute ethanol; $[\alpha]_D^{20}$ +24.5°, chloroform).

The known substances were identified by direct comparison of their physicochemical properties, melting points, mixed melting points, and R_f values in a number of systems on parallel chromatography with authentic samples and from their IR spectra. The properties of the 6-isopentenyloxy-5-methoxyangelicin were compared with those described by Dreyer [2].

Heraclesol (I). The substance isolated consisted of faintly yellowish crystals with mp 117-118°C, $[\alpha]_D^{20}$ +30° (methanol), $C_{17}H_{18}O_7$. It was detected in paper chromatography in the form of a dark brown spot with R_f 0.35 (benzene–formamide). The PMR and UV spectra are described in the discussion of the results.

Hydrolysis of Heraclesol (I) to 6-Hydroxy-5-methoxyangelicin (II). A solution of 30 mg of the substance in 1 ml of acetic acid containing sulfuric acid (one drop of sulfuric acid was added to 10 ml of acetic acid) was left for a day. The yellowish crystals of (II) that deposited (12 mg) melted at 223-224°C and had the empirical formula $C_{12}H_8O_5$. Substance (II) proved to be identical with 6-hydroxy-5-methoxyangelicin – the product of the hydrolysis of 6-isopentenyloxy-5-methoxyangelicin (V).

Heraclesol Acetonide (III). A solution of 10 mg of heraclesol (I) in 20 ml of anhydrous acetone was treated with 50 mg of anhydrous copper sulfate and the reaction mixture was boiled for 2 h with periodic monitoring of the course of the reaction by paper chromatography in the petroleum ether – formamide system (R_f of the acetonide 0.6). After this, the copper sulfate was separated off, the acetone was distilled off, and the residue (11 mg) was crystallized from ethanol. The acetonide (III) obtained had mp 114-115°C, $[\alpha]_D^{20}$ +10° (c 0.2; methanol) and the empirical formula $C_{20}H_{20}O_7$. The absorption maxima in the UV spectrum corresponded to those of the initial substance.

Methylation of 6-Hydroxy-5-methoxyangelicin (II) to Pimpinellin (IV). Substance (II) (10 mg) was dissolved in 3 ml of a solution of diazomethane in diethyl ether. After the disappearance of the yellow coloration, a solution of diazomethane was added to the reaction mixture dropwise until the yellow coloration had been restored. Then the ether with the remains of the diazomethane that had not reacted was distilled off and the residue was crystallized from ethanol. This gave 7 mg of acicular crystals (mp 148-151°C, empirical formula $C_{13}H_6O_5$), identical with pimpinellin [4].

SUMMARY

The roots of Lesko's cow parsnip have yielded 13 substances of coumarin nature: osthole, psoralen, bergapten, xanthotoxin, isopimpinellin, phellopterin, heracol, biacangelicin, angelicin, sphondin, isobergapten, 6-isopentenyloxy-5-methoxyangelicin, and heraclesol.

Heraclesol is a new compound and is (+)-6-[2(R)3-dihydroxy-3-dimethylbutoxy]-5-methoxyfuro-2',3':7,8-coumarin (I), and this is the first time that 6-isopentenyloxy-5-methoxyangelicin has been obtained from a plant of the genus *Heracleum*.

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OSCILLOPOLAROGRAPHY OF RUTIN

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Rutin – vitamin P – is a natural flavonoid glucoside. There is information in the literature on the classical polarography of rutin [1, 2]. Oscillopolarography has advantages and greater possibilities.

We have studied the oscillopolarographic behavior of pure rutin under various conditions. We investigated pure rutin with mp 189-191°C on an OP-03 oscillopolarograph with a dropping mercury electrode. The comparison electrode was a saturated calomel electrode. The supporting electrolytes were acetate – ammonium buffer solutions at pH 3-8. The rutin solution was prepared in 96% ethanol. The rutin solution to be polarographed contained, after dilution, 8% of ethanol in a 0.1 N solution of the supporting electrolyte. The measurements were performed with linear and triangular voltage sweeps.

On a support of the buffer solutions mentioned, with an increase in the pH at a constant concentration of rutin a shift in the reduction potential (E_r) in the negative direction was observed:

$-E_r$	1,25	1,35	1,41	1,55	1,60	1,63	1,70	1,80
pH	3	4	5	6	7	8	9	10

$$\frac{\Delta E}{\Delta \mathrm{pH}} = 72\,\mathrm{mV/pH}$$

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