COUMARINS OF THE ROOTS OF Seseli iliense

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The roots of Seseli iliense (Regel et Schmalh) Lipsky, according to thin-layer chromatography on Silufol in the petroleum ether–ethyl acetate (1 : 1) system, contain three coumarin derivatives giving spots with R_f 0.68, 0.56, and 0.63. When an extract of the roots was chromatographed on silica gel, all these substances were isolated. The compounds with R_f 0.68 having the composition $C_{21}H_{22}O_4$ and mp 127-128°C and with R_f 0.53 having the composition $C_{21}H_{22}O_4$ with mp 72-73°C are new; they have been called iselin and iliensin, respectively. The substance with R_f 0.56 is identical with peucenol [1].

The UV spectrum of iselin [λ_{max}^{EtOH} 221.5; 244 infl.; 251; 260; 268.5; 311 nm (log ε 4.50; 4.32; 4.36; 4.33; 4.32; 4.24); λ_{min} 236; 257; 265; 278.5 nm (log ε 4.25; 4.32; 4.30; 3.85)] shows that the substance belongs to the group of linear furocoumarins with a O-alkyl substituent in position 5. Its IR spectrum (Fig. 1) confirms this conclusion: bands at 3170 and 3130 cm^{-1} are due to the vibrations of C–H group of a furan nucleus, at 3075 cm^{-1} to the C–H vibrations of benzene and α pyrone rings, at 1722 cm^{-1} to the C=O of an α-pyrone ring, and at 1624, 1605, 1579, and 1545 cm^{-1} to the C=C bond of aromatic and heteroaromatic rings. The number of intensities of the bands in the 1500-1650 cm^{-1} range also characterize iselin as a furocoumarin with a O-alkyl substituent in position 5 [2].

The features of the NMR spectrum (Fig. 2) agree completely with the conclusion drawn: doublets at 6.19 and 8.04 ppm, J = 9.5 Hz, are due to the H_3 and H_4 protons, a singlet at 7.05 ppm to the H_8 protons, and doublets at 6.91 and 7.52 ppm, J = 2.5 Hz, to the $H_{4'}$ and $H_{5'}$ protons. As has been mentioned previously [3, 4], when there is a substituent in position 5 of coumarin derivatives there is a paramagnetic shift of the H_4 signal to approximately 8 ppm, as is observed in the present case.

Thus, the UV, IR, and NMR spectra of iselin show that it is an ether of bergaptol. The acid hydrolysis of iselin confirms these conclusions: the substance obtained on hydrolysis was identical with bergaptol in its melting point, and the mixed melting point and IR spectrum.

The structure of the O-alkyl substituent, $C_{10}H_{17}$, follows from a consideration of the signals in the NMR spectrum of iselin that are not due to the bergaptol residue. A 2-proton singlet at 4.85 ppm, $W_{1/2}$ 2.5 Hz is due to the methylene protons in a $Ar-O-CH_2-C=C$ grouping, a 2-proton multiplet at 2.16 ppm, $W_{1/2}$ = 17 Hz to the methylene protons in a $CH_2-CH_2-C=C$ grouping, a 2-proton singlet at 1.75 ppm, $W_{1/2}$ 6 Hz, to the protons of a methylene group located between a double bond and quaternary carbon atom ($-\overset{|}{\underset{|}{C}}-CH_2-C=C$), a three-proton singlet at 1.62 ppm, $W_{1/2}$ 5 Hz to the protons of a methyl group located on a double bond ($CH_3-C=C$), a 2-proton triplet at 1.37 ppm, J = 6.5 Hz, to the protons of a methylene group located between another methylene group and a quaternary carbon atom ($-\overset{|}{\underset{|}{C}}-\underline{CH_2}-CH_2$), and a 6-proton singlet at 0.86 ppm to the protons of two methyl groups attached to a quaternary carbon atom. This corresponds to one of two possible variants of the structure of the O-alkyl substituent $C_{10}H_{17}$ – (I) or (II):

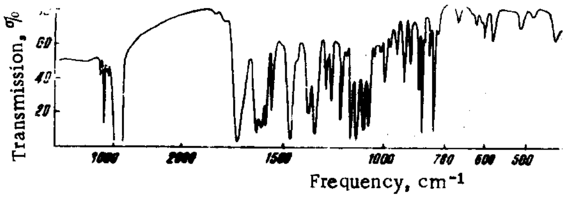

Fig. 1. IR spectrum of iselin.

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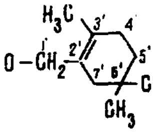

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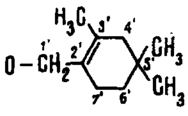

II

The double resonance spectra (see Fig. 2) confirm the assignments made and the proposed structure of the O-alkyl substituent. The protons of the methylene group of a double bond [4' in (I) or 7' in (II)] interact with a constant of 6.5 Hz with the protons of the methylene group at 5' or 6' (δ 1.37 ppm), as follows from the INDOR spectrum. Simultaneously, a long-range interaction of these groups with $C_{3'}-CH_3$ and $O-CH_2$ is observed; as a result, it appears in the spectrum in the form of a broad signal at 2.16 ppm with $W_{1/2}$ 17 Hz. Furthermore, the groups $O-CH_2$, $CH_3-C=C$ and $-C-CH_2C=C$ interact with one another with small constants, which also leads to the broadening of their signals. The increase in the height of the singlet from $O-CH_2$ (4.85 ppm) when the transitions of the CH_3 and CH_2 groups of the substituent are irradiated provides the possibility of making a choice between structures (I) and (II).

In actual fact, the interaction of $O-CH_2$ with the protons of the CH_2 group in position 7' (through four bonds) must be more considerable than with the CH_2 group in position 4' (through five bonds). In this case, differences in the orientation of the protons do not play a fundamental role, since as the result of the rapid

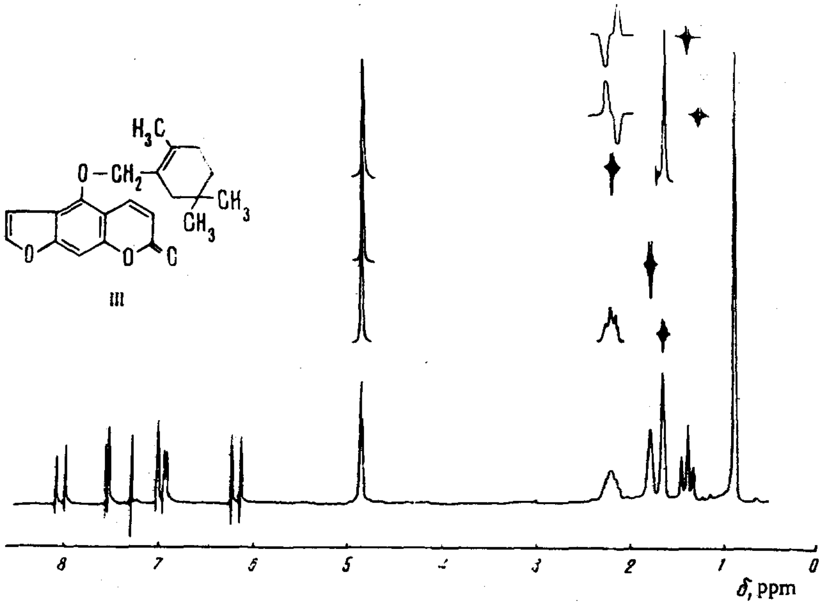

Fig. 2. NMR spectrum of iselin.

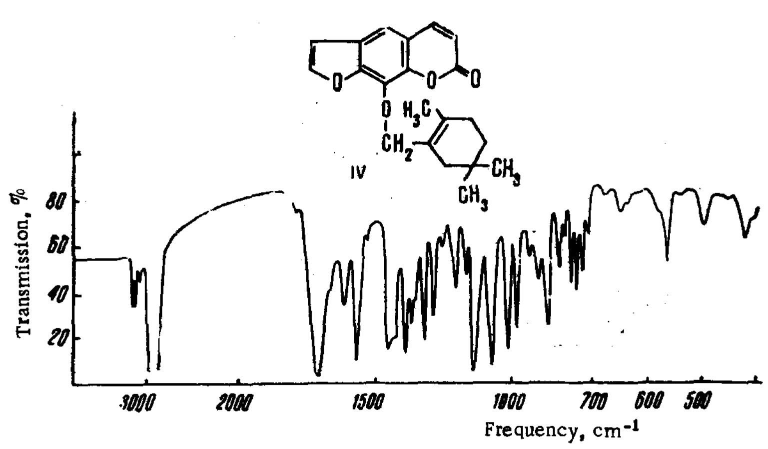

Fig. 3. IR spectrum of iliensin.

TABLE 1. Characteristics of the NMR Spectrum of Iliensin

Chemical shift, δ, ppm	Multiplicity, J, Hz	Intensity	Assignment
6,27	d., 9,5	1H	H_3
7,69	d., 9,5	1H	H_4
7,28	s.	1H	H_5
6,74	d., 2,5	1H	$H_{4'}$
7,61	d., 2,5	1H	$H_{5'}$
4,91	s., $W_{\frac{1}{2}}$ 2,5	2H	$Ar-O-CH_2-C=C-$
2,16	m, $W_{\frac{1}{2}}$ 16,0	2H	CH_2-C-C-
1,64	s., $W_{\frac{1}{2}}$ 5,0	2H	$C-CH_2-C-C-$
1,56	s., $W_{\frac{1}{2}}$ 5,0	2H	CH_3-C-C-
1,30	t., 6,5	2H	$-C-\underline{CH_2}-CH_2-$
0,84	s	6H	$(CH_3)_2C<$

conversion of the ring an averaged spectrum is observed. It can be seen from Fig. 2 that when the singlet at 1.75 ppm is irradiated, the intensity of the signal at 4.85 ppm rises to a greater extent than when the transitions of the other groups are irradiated. Thus, the isolated CH_2 group is present in position 7', and the O-alkyl substituent has structure (I).

The IR spectrum of iliensin [λ_{max}^{EtOH} 219, 245 infl., 250, 265, 302 nm (log ε 4.51, 4.42, 4.44, 4.22, 4.17); λ_{min} 233, 263, 277 nm (log ε 4.27, 4.21, 3.92)] is characteristic for linear furocoumarins with a O-alkyl substituent in position 8. The features of the IR spectrum of the substance (Fig. 3) lead to the same conclusion: bands at 3145 at 3120 cm^{-1} are due to the C–H vibrations in the furan ring, a band at 3075 cm^{-1} to the C–H vibrations of benzene and α-pyrone rings, at 1720 cm^{-1} to the C = H bond of an α-pyrone ring, and at 1622 and at 1586 cm^{-1} to the C = C bonds of aromatic and heteroaromatic rings.

The NMR spectrum of iliensin (Table 1) confirms its structure as 9-monosubstituted linear furocoumarin and shows the identity of the substituent in position 9 to the substituent in iselin. The acid hydrolysis of iliensin gives xanthotoxol. Thus, iliensin has the structure shown in Fig. 3.

As compared with other species of Seseli, the presence of compounds with the cycloalkyl substituent (I) is characteristic for S. iliense, this substituent having been found previously only in one coumarin derivative – peucenol, isolated from Peucedanum morisonii Bess. [5, 6].

EXPERIMENTAL

The analytical results corresponded to the calculated figures.

For the chromatographic separation of the substances, we used silica gel L 40/100 μ. The thin-layer chromatography of the substances was performed on Silufol in the petroleum ether–ethyl acetate (1 : 1) system. The IR spectra of the substances in paraffin oil were taken on a UR-10 spectrometer, the UV spectra of solutions in ethanol on a Hitachi EPS-3T spectrophotometer, and the NMR spectra of solutions in $CDCl_3$ at 25°C (O–HMDS) on a Varian HA-100 D spectrometer. The melting points of the substances were determined on a Kofler block.

Total Coumarins. The finely-comminuted roots of Seseli iliense collected in the Dzhungarian Ala-Tau (Taldy-Kurgan oblast, Kazakhstan) (1 kg) were extracted with petroleum ether (1.5 + 3 × 1 liter), and the extract was evaporated. This gave 51.7 g of an oily residue. Then the raw material was extracted with acetone (3 × 1 liter). Evaporation of this extract gave 45.0 g of an oily residue.

Iselin. The petroleum-ether extract (51.7 g) was adsorbed on 250 g of silica gel and transferred to a column (96 × 180 nm) containing 500 g of silica gel. Fractions 1-7 were eluted with petroleum ether, fractions 8-37 with petroleum ether–ethyl acetate (95 : 5), 38-97 with petroleum ether–ethyl acetate (90 : 10), fractions 98-105 with petroleum ether–ethyl acetate (75 : 25), and then fractions 106 and 107 with ethyl acetate, the volume of each fraction being 350 ml.

Fractions 27-37 yielded 530 mg of colorless crystals with the composition $C_{21}H_{22}O_4$, mp 127-128°C [ethyl acetate–petroleum ether (4 : 1)]. When subjected to TLC on Silufol, the substance gave a single spot with R_f 0.68 fluorescing yellow-green in UV light (365 nm).

Iliensin. Fractions 62-67 yielded 3.42 g of colorless crystals with the composition $C_{21}H_{22}O_4$, mp 72-73°C (from ethyl acetate). When subjected to TLC on Silufol, the substance gave a single spot with R_f 0.53 fluorescing yellow-green in UV light (365 nm).

Peucenol. Fractions 86-92 yielded 300 mg of colorless crystals with mp 146-147°C. When subjected to TLC on Silufol, the substance gave a single spot with R_f 0.56 [violet fluorescence on irradiation with ultraviolet light (365 nm)]. From its IR and NMR spectra the substance was identical with peucenol; a mixture with an authentic sample of peucenol gave no depression of the melting point. The chromatography under similar conditions of the acetone extract (45.0 g) yielded an additional 1.42 g of peucenol.

Hydrolysis of Iselin. A solution of 100 mg of iselin in 0.5 ml of acetic acid was treated with 0.05 ml of sulfuric acid and heated at 80°C for 10 min. The light-yellow crystalline precipitate that deposited was separated off and washed with 1 ml of ether. This gave 33 mg of a substance with mp 278-280°C identical in its IR spectrum and a mixed melting point with bergaptol.

Hydrolysis of Iliensin. A solution of 150 mg of iliensin in 0.75 ml of acetic acid was treated with 0.1 ml of concentrated sulfuric acid. After 30 min, the light-yellow crystals that had deposited were separated off and washed with 1 ml of ether. Yield 63 mg, mp 244-245°C. From its IR spectrum and a mixed melting point, the substance was identical with xanthotoxol.

CONCLUSION

From the roots of *Seseli iliense* (Regel et Schmalh) Lipsky, in addition to the coumarin peucenol, two new furocoumarins have been isolated – iselin and iliensin. The most probable structures of these compounds has been proposed on the basis of the results of the characteristics of their UV, IR, and NMR spectra.

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