FLOROSELIN, A NEW COUMARIN FROM THE ROOTS OF Seseli sessiliflorum

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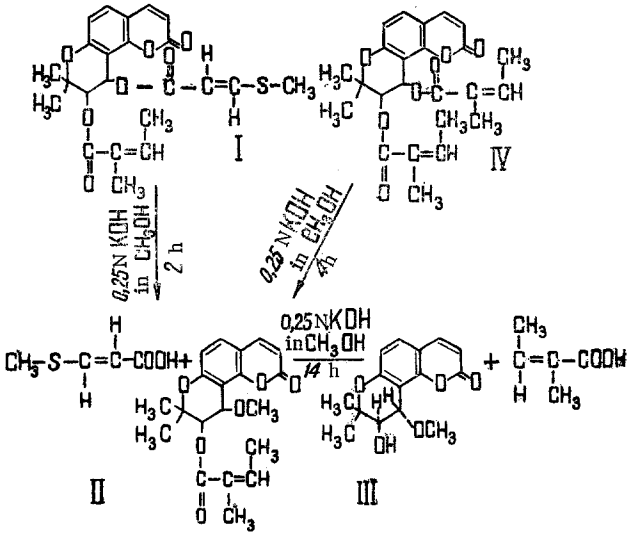
From a methanolic extract of the roots of Seseli sessiliflorum Schrenk. we have isolated a new coumarin with the composition $C_{23}H_{24}O_7S$, mp 161.5-163°C (from ethanol), $[\alpha]_D^{21}$ – 121.2° (chloroform), which we have called "floroselin" (I). The fact that I is a coumarin was shown by its UV spectrum [λ_{max}, nm: 256, 294, and 320 (inflection) (log ε 3.70, 4.32, and 4.12)] and its IR spectrum [1730 cm^{-1} (C=O of an α-pyrone), 1607 and 1570 cm^{-1} (–C=C bond of an aromatic system)] (Fig. 1).

As the NMR spectrum of I (Fig. 2) shows, its structure is based on a 7,8-disubstituted coumarin nucleus (H_3, 6.19 ppm; H_4, 7.58 ppm, doublet; J = 10.0 Hz; H_5, 7.35 ppm; and H_6, 6.79 ppm, doublet; J = 8.5 Hz) [1] condensed with a 2',2'-dimethyl-3',4'-dihydropyran ring having two alkoxy groups in the 3' and 4' positions (gem-dimethyl group, 1.44 and 1.49 ppm, singlet, 3H each; $H_{3'}$, 5.43 ppm; and $H_{4'}$, 6.65 ppm, doublet, J = 5.0 Hz) [2, 3]. The latter situation is confirmed by the presence in the IR spectrum of I of bands at 1730 and 1700 cm^{-1} (the first with an increased intensity) and also by the capacity of I for undergoing saponification.

One of the acid residues is angeloyl. In the NMR spectrum of I there is the characteristic six-proton multiplet in the range from 1.8-2.0 ppm and a one-proton multiplet with the center at 6.05 ppm [4].

The mild alkaline methanolysis of I gave compound II with the composition $C_{20}H_{22}O_6$, mp 92-94°C (from petroleum ether) whose NMR spectrum (Fig. 3) lacks the singlet at 2.37 ppm (3H) and the one-proton doublets with δ 5.77 and 7.08, J = 10.0 Hz, due to the second acyl residue that was present in the NMR spectrum of I. The appearance of a singlet at 3.80 ppm (3H) shows that this residue has been replaced by a methoxy group.

Scheme of the chemical transformations of floroselin



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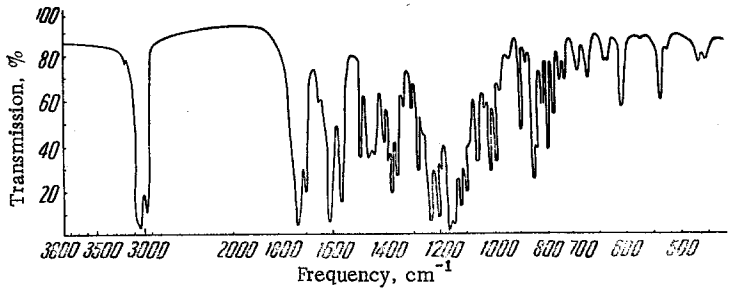


Fig. 1. IR spectrum of floroselin (mull in paraffin oil).

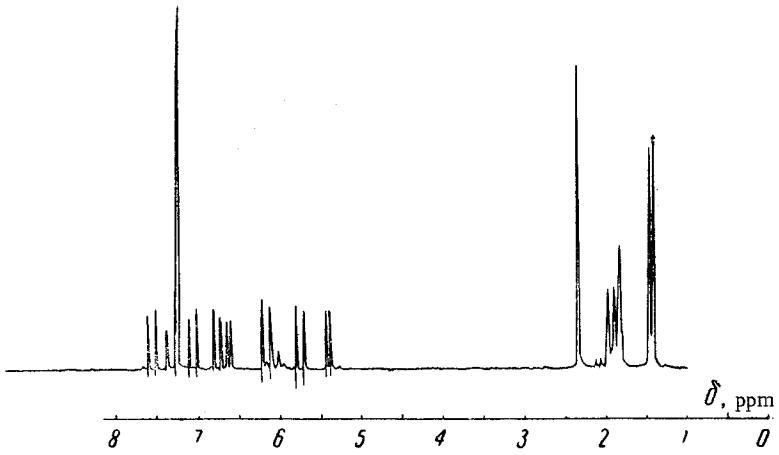


Fig. 2. NMR spectrum of floroselin (in $CDCl_3$).

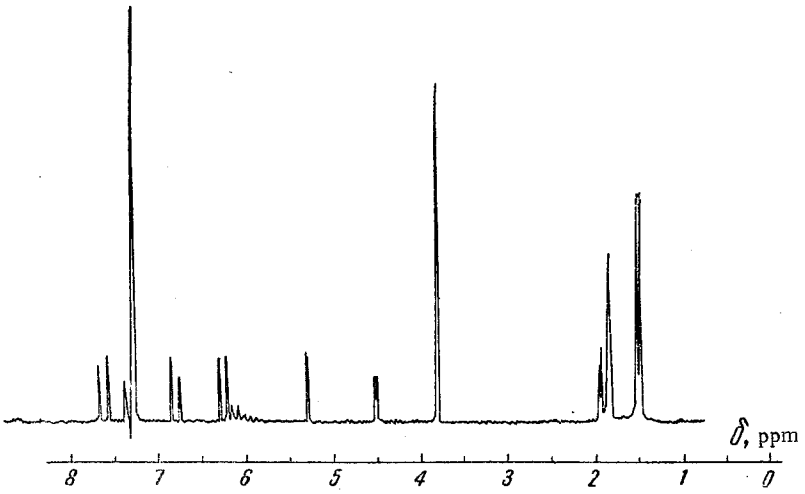
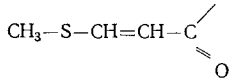


Fig. 3. NMR spectrum of II, the product of incomplete alkaline methanalysis of floroselin (in $CDCl_3$).

By comparing the empirical formulas of I and II and taking into account the appearance of a methoxy group in the latter, we see that the acid residue has the composition C_4H_5OS. In the IR spectrum of II the carbonyl band at 1700 cm^{-1} has disappeared. These results permit us to propose the structure of 3-methylthioacryloyl for the second acyl residue.



The NMR and IR spectra of the isolated acid [S−CH_3, 2.42 ppm, singlet, 3H; and 7.19 and 5.87, doublet, J = 10.0 Hz, 1H each; $\nu_{C=O}$ 1683 cm^{-1}] confirm this conclusion. The melting point (121.5-122°C) makes it possible to identify it as trans-3-methylthioacrylic acid (mp 124°C) [5].

The equality of the coupling constants of the olefinic protons of free trans-3-methylthioacrylic acid and of the corresponding acyl residue in I excludes the isomerization of the acid during the saponification process.

The positions of the acyl residues in I are derived from the structure of II established by its NMR spectrum, in which the signal from H_4' is shifted upfield by 2.15 ppm (δ 4.50 ppm, J = 2.0 Hz), and the signal from H_3' by 0.14 ppm (δ 5.29 ppm, J = 2.0 Hz). The assignment of the signals from H_3' and H_4' was made on the basis of the spectra of model compounds [6] and also from the broadening of the H_4' signal due to long-range spin−spin coupling with the aromatic protons [7, 8].

Consequently, the trans-3-methylthioacrylic acid residue that is split out is present in position 4'. This conclusion is in agreement with literature information on the saponification of diesters of dihydrofuro- and dihydropyranocoumarins in which, during the first stage, the acyl residue in the position α to the aromatic nucleus splits out and is replaced by a methoxy group [9-11].

The signals ascribed to the protons of angelic acid are retained in the NMR spectrum of II, which shows the presence in this product of an angeloyloxy group occurring in position 3'.

Further saponification of II in alkaline methanol gave (+)-trans-methylkhellactone, $C_{15}H_{16}O_5$, mp 160-162°C, $[\alpha]_D^{21}$ +88.3° (ethanol), III, and angelic acid with mp 42-43°C.

To confirm this conclusion concerning the structure of II, we subjected anomalin (IV) to partial hydrolysis and obtained a compound identical with II.

Thus, substance II has the structure of 3'-angeloyloxy-4'-methoxy-2',2'-dimethyl-3',4'-dihydropyrano-5',6':8,7-coumarin, and floroselin is 3'-angeloyloxy-2',2'-dimethyl-4'-(trans-3-methylthioacryloyloxy)-3',4'-dihydropyrano-5',6':8,7-coumarin (I).

EXPERIMENTAL

The UV spectra were taken on an SF-4A spectrophotometer in ethanol, the IR spectra on a UR-10 spectrophotometer (mulls in paraffin oil), and the NMR spectra on a HA-100D (100 MHz) instrument in $CDCl_3$ (internal standard, TMS). Mass spectrometric determination of the molecular weight was carried out by P. I. Zakharov and the microanalyses by E. A. Nikonova. The elementary analyses of all the compounds corresponded to the calculated figures.

Isolation of Floroselin. A 1.2-kg sample of the dried and comminuted roots of Seseli sessiliflorum was extracted with methanol (3 × 5 liters). The combined extracts (10.8 liters), evaporated to 220 ml, were diluted with a double volume of water and were treated with ether (10 × 250 ml). The ethereal extracts were washed with 5% sodium carbonate solution (5 × 100 ml), and then with water (3 × 100 ml) and dried over Na_2SO_4, and the solvent was evaporated off in vacuo. The oily residue (67 g) was dissolved in 200 ml of a mixture of ethyl acetate and petroleum ether (1 : 2). On standing the solution deposited 2.4 g of a crystalline substance with mp 161.5-163°C (from ethanol), $[\alpha]_D^{21}$ − 121.2° (c 0.33, chloroform). Found %: C 61.90, 62.27; H 5.45, 5.46; S 6.93, 7.13. Mol. wt. 444 (mass spectrometry). $C_{23}H_{24}O_7S$. Calculated %: C 62.14; H 5.44; S 7.21. Mol. wt. 444.49.

Stepwise Alkaline Methanolysis of Floroselin (first stage). Isolation of II. A mixture of 0.7 g of floroselin and 30 ml of a 0.25 N solution of KOH in methanol was left at room temperature for 2 h. Then it was diluted with a double volume of water, acidified with 10% H_2SO_4, and treated with ether (5 × 10 ml). The ethereal extracts were washed with 1% sodium carbonate solution and then with water (3 × 10 ml) and dried over Na_2SO_4, and the solvent was distilled off in vacuo. The residue obtained by preparative separation in a thin layer of acidic alumina (Brockmann activity grade II) in an ethyl acetate−petroleum ether system (1 : 4) yielded 0.15 g of a substance $C_{20}H_{22}O_6$, mp 92-94°C, mol. wt. 358 (mass spectrometry), and also 0.2 g of the initial substance I that had not reacted.

Isolation of trans-3-Methylthioacrylic Acid. The combined extracts obtained on washing the ethereal extract of the total hydrolysis products with sodium carbonate solution were acidified with 10% H_2SO_4, saturated with sodium chloride, and treated with ether (4 × 25 ml). The ethereal extracts were dried over

Na_2SO_4 and evaporated in vacuo. The residue was found by chromatography on paper in butan-1-ol saturated with 1.5 N NH_3 solution and subsequent treatment with a 0.2% phenolic solution of bromphenol blue to contain an acid with R_f 0.24. The acid fraction (0.1 g) was sublimed in vacuo with water-bath heating. This gave fine-colorless acicular crystals with mp 121.5-122°C.

Saponification of Floroselin (second stage). Isolation of III. Substance II was left to stand in 30 ml of a 0.25 N methanolic solution of KOH for 14 h. Then the reaction mixture was treated as described for the first stage of the saponification of I. The ethereal extracts yielded a substance with mp 160-162°C, $[\alpha]_D^{21}$ + 88.3° (c 0.48, ethanol), whose IR spectrum was identical with that of trans-methylkhellactone. A mixture with an authentic sample of trans-methylkhellactone showed no depression of the melting point.

Isolation of Angelic Acid. By the method described for the first stage of the alkaline methanolysis of I, the acid fraction yielded an acid with mp 42-43°C. A mixture with an authentic sample of angelic acid gave no depression of the melting point. The IR spectra of the isolated acid and of the authentic sample of angelic acid were identical.

Alkaline Methanolysis of Anomalin. A mixture of 0.3 g of anomalin and 30 ml of a 0.25 N methanolic solution of KOH was left at room temperature for 4 h. Then the reaction mixture was worked up as described for the first stage of the saponification of floroselin. By preparative separation in a thin layer of acidic alumina (Brockmann activity grade II) in an ethyl acetate–petroleum ether system (1:4), the lactone fraction yielded 0.10 g of a substance with mp 92-94°C whose mixture with II showed no depression of the melting point. The IR spectra of the two substances coincided completely.

CONCLUSIONS

A new coumarin has been isolated from the roots of Seseli sessiliflorum for which the structure of 3'-angeloyloxy-2',2'-dimethyl-4'-(trans-3-methylthioacryloyloxy)-3',4'-dihydropyrano-5',6':8,7-coumarin has been proposed. This is the first time that esters of 3-methylthioacrylic acid have been found in the coumarin series.

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