GOSFEROL – A NEW FUROCOUMARIN FROM THE ROOTS OF *Prangos ferulacea*

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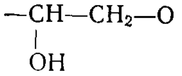
In a study of the coumarin compounds from the roots of Prangos ferulacea (L.) Lindl., collected in the Bichenak mountains of the Nakhichevan ASSR, we isolated a substance (I) of mol. wt. 286 (mass spectrometrically) with the composition $C_{16}H_{14}O_5$, mp 136.5-138.5°C.

Substance (I) possesses the properties characteristic of coumarin derivatives and gives a UV spectrum in which there are absorption maxima at 222, 250, 258, 266, and 310 nm (log ε 4.19, 4.24, 4.09, 4.16, and 4.04, respectively), which indicate that (I) belongs to the group of 5-monosubstituted furocoumarins.

The IR spectrum of (I) shows characteristic absorption bands at (cm^{-1}) 3455 (OH), 1715 (C=O of an α-pyrone ring), 1630, 1610, 1585, and 1555 (aromatic nucleus). The UV and IR spectra of (I) coincide completely with those described previously [1] for (±)-pranferol. A mixture of authentic samples of the substances mentioned gave no depression of the melting point, which shows their identity. However, the chemical composition of (I) differs from that proposed [1] for (±)-pranferol by two hydrogen atoms. Previously [1], on the basis of a study of spectral and chemical characteristics, the molecular formula $C_{16}H_{16}O_5$ was found for pranferol, and the structure 5-(2''-hydroxy-3''-methylbutoxy)furo-2',3':7,6-coumarin was proposed for it.

In order to refine the structure of (I), we have compared the NMR and mass spectra. In the NMR spectrum of (I) (Fig. 1, I) in the region of aromatic protons there are four doublets with chemical shifts of δ 6.19, 8.11 (J = 9.7 Hz), 6.91, and 7.48 (J = 2.8 Hz) due to the 3,4-protons of the coumarin nucleus and the 4',5'-protons of the furan nucleus. The singlet at δ 7.07 ppm is due to the proton in position 8. This assignment is confirmed by the long-range spin–spin coupling constants observed on recording with a broad scan ($J_{4',8} \approx J_{1',8} \approx 0.7$ Hz). As is well-known, such splitting is absent for H-5. Consequently, the side chain is present in position 5. In the region of olefinic protons there are singlets with δ 5.01 and 5.17 ppm with intensities of one proton unit each, apparently due to the protons of a CH_2 group. These singlets are broadened because of geminal interaction and interaction with a CH_3 group (shown by double resonance). This group is represented by a broadened signal at δ 1.81 ppm with an intensity of three proton units. The multiplet in the δ 4.25-4.60 ppm range of three proton units may be ascribed to a $-CH-CH_2-O-Ar$ group. A doublet with δ 2.33 ppm ($J_{CHOH} = 3.5$ Hz) with an intensity of one proton unit is due to the proton of an OH group attached to a saturated carbon atom. (The signal shifts with a fall in the temperature.) It was shown by means of double resonance that the splitting of this signal is due to interaction with the methine proton in a



$$\underset{\displaystyle OH}{\overset{|}{-CH}}-CH_2-O$$

grouping.

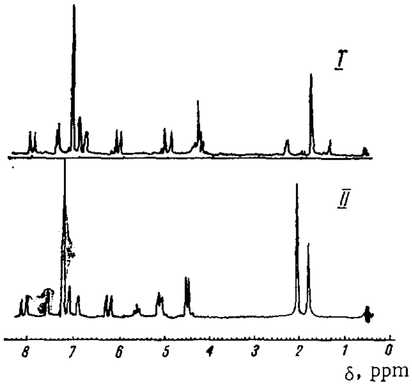


Fig. 1. NMR spectrum of gosferol (I) and its acetate (II).

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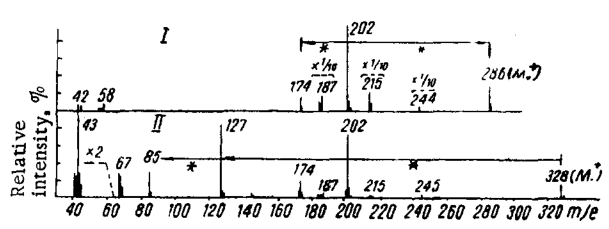
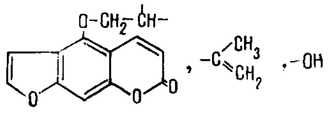


Fig. 2. Mass spectrum of gosferol (I) and its acetate (II).

What has been said above shows that the molecule of (I) has fragments from which the following structure for (I) unambiguously follows:



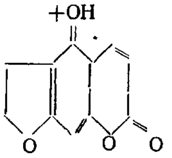
The facts given agree well with the results of chemical and mass-spectrometric investigations.

The acetylation of (I) with acetic anhydride in pyridine formed the acetyl derivative (II) with mp 121-122°C, the IR spectrum of which lacked the absorption band of a hydroxy group and showed, in addition to the band at 1725 cm^{-1} (C=O of an α-pyrone ring), an absorption band at 1740 cm^{-1} (C=O group of an ester). The NMR spectrum of (II) (Fig. 1, II) showed an additional singlet from $COCH_3$ at δ 2.10 ppm (3 H).

The treatment of (I) with 20% sulfuric acid gave a substance (III) with mp 146.5-147°C, identical with a known furocoumarin — isooxypeucedanin according to a mixed melting point and the similarity of their IR spectra. The nature of the isomerization taking place under these conditions shows that there is a $-\underset{\displaystyle OH}{CH}-C{\overset{\displaystyle CH_3}{\diagup}\atop\underset{\displaystyle CH_2}{\diagdown}}$ grouping in the side chain of (I) [2]. Compound (III) is also formed by the oxidation of (I) with chromium trioxide in glacial acetic acid [1]. Apparently, in a dense medium in addition to the oxidation of the secondary OH group, the migration of hydrogen atoms takes place with the formation of isooxypeucedanin.

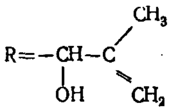
The hydrogenation of (I) with Pt (in the form of PtO_2) leads to substance (IV) with mp 105.5-106°C. From the similarity of their IR spectra and by means of a mixed melting point of authentic samples, this was identified as pranferol, which agrees well with the presence of a $-C{\diagup CH_3 \atop \diagdown CH_2}$ grouping in the side chain of (I). Substance (IV) forms an acetyl derivative (V) with mp 111-112°C. In addition to (IV), a substance (VI) with mp 109.5-110.5°C and (VIII) with mp 161-163°C were isolated from the products of the hydrogenation of (I).

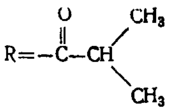
In UV light compound (VI) possesses a violet fluorescence, which shows that in the hydrogenation of (I) not only the double bond in the side chain but also the double bond in the furan ring is reduced, since this fluorescence is characteristic of dihydrofurocoumarins. This is confirmed by the mass spectrum of (VI), which clearly shows the molecular ion M^+ with m/e 290 and the peak of a fragment with m/e 204.

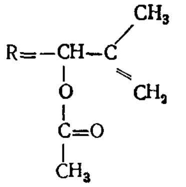


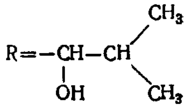
[Compare the formation of fragment *a* with m/e 202 in the decomposition of (I).] The IR spectrum of (VI) has absorption bands at (cm^{-1}) 3400 (OH group), 1695 and inflection at 1715 (C=O of an α-pyrone ring), 1620, 1610, and 1580 (aromatic nucleus). The presence of an OH group is confirmed by the formation of an acetate (VII) with mp 117-118°C.

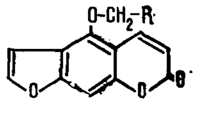
In UV light, substance (VIII) has a bright blue fluorescence and it gives an IR spectrum showing absorption bands at (cm^{-1}) 3250, 3480 (OH group), 1675 (C=O of a carboxy group), and 1590, 1575 (aromatic ring). The structure of (VIII) has not yet been established.

I.

$R=-CH(OH)-C(=CH_2)CH_3$

III.

$R=-C(=O)-CH(CH_3)_2$

II.

$R=-CH(OCOCH_3)-C(=CH_2)CH_3$

IV.

$R=-CH(OH)-CH(CH_3)_2$



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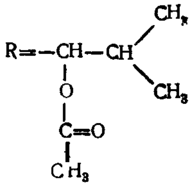
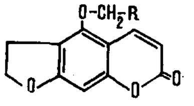
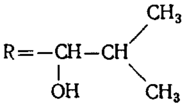
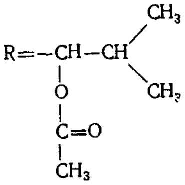

$R=-CH(OCOCH_3)-CH(CH_3)_2$

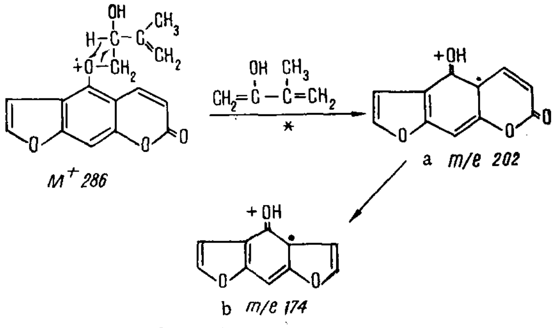


VI.

$R=-CH(OH)-CH(CH_3)_2$

VII.

$R=-CH(OCOCH_3)-CH(CH_3)_2$

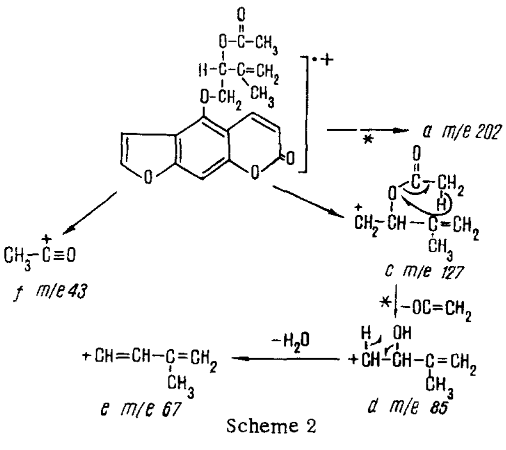
The features of the structure of (I) also appear in its fragmentation under electron impact (Scheme 1). The main process of the decomposition of (I) is determined by an energetically favorable rearrangement with the migration of an atom of hydrogen through a four-membered transition state to an oxygen atom with the formation of fragment *a* with m/e 202 and the neutral molecule 2-hydroxy-3-methylbutadiene $CH_2=C(OH)-C(CH_3)=CH_2$.

The expulsion of carbon monoxide from the α-pyrone ring that is characteristic for coumarin derivatives then leads to the appearance of an ion b with m/e 174.



Scheme 1

The decomposition of the acetate (II) takes place in two competing directions (Scheme 2). On the one hand, there is the formation of ion *a* with m/e 202, and on the other hand the cleavage of the $-O-CH_2-$ bond, giving the ion c with m/e 127. The subsequent decomposition of fragment c takes place with the successive ejection of ketene and water to form fragments d and e with m/e 85 and 67. The maximum peak in the spectrum is the peak of fragment f with m/e 43.



Scheme 2

EXPERIMENTAL

Isolation of Gosferol (I). The mixture of crystalline substances (3 g) obtained from fractions 22 and 23 after the isolation of pranferol [3] and pranferin [4] was chromatographed on alumina (50 g, activity grade II). Elution was performed with benzene, benzene–chloroform (2 : 1 and 1 : 1), and chloroform. The volume of each fraction was 50 ml. Elution with the mixed solvent gave (I), $C_{16}H_{14}O_5$, with mp 136.5-138.5°C (from ethanol), α_D^{20} ± 0° (chloroform), R_f 0.62 (Al_2O_3, activity grade II, ethyl acetate system). Yield 1.5 g.

Found, %: C 67.24; 67.11; H 5.0; 5.10. M 286 (mass-spectrometrically). $C_{16}H_{14}O_5$. Calculated, %: C 67.13; H 4.88. M 286.

Acetylation of (I). A mixture of 0.1 g of (I), 2 ml of acetic anhydride, and 0.5 ml of pyridine was heated for 2 h. Then it was diluted with water and worked up in the usual way. This gave 0.075 g of the acetyl derivative (II) with mp 121-122°C (from petroleum ether), R_f 0.62 [Al_2O_3, activity grade II, ethyl acetate–benzene (1 : 4) system].

Action of H_2SO_4 on (I). A solution of 0.0541 g of (I) in 5 ml of ethanol was treated with 10 ml of 20% H_2SO_4 and heated in the water bath for 3 h. The reaction products yielded 0.04 g of substance (III) with mp 146.5-147°C (from ethanol), identified as isooxypeucedanin.

Hydrogenation of (I). The exhaustive hydrogenation of 0.1025 g of (I) was performed in 50 ml of ethanol over a platinum catalyst. The catalyst was filtered off and washed with ethanol. Distillation of the filtrate yielded 0.095 g of a residue consisting of three substances. The preparative separation of this mixture in a thin layer of alumina (activity grade II) in the ethyl acetate–benzene (1 : 2) system gave 0.05 g of (IV) with mp 105-106°C (from benzene), identified as pranferol; 0.02 g of (VI) with mp 109.5-110.5°C [from benzene–petroleum ether (1 : 1)], and 0.015 g of (VIII) with mp 161-163°C (from petroleum ether).

Acetylation of (IV). A mixture of 0.03 g of (IV), 2 ml of acetic anhydride, and 0.5 ml of pyridine was heated for 2 h. Then it was cooled, diluted with water, and extracted with ether. The ethereal extracts were washed with water and dried with anhydrous sodium sulfate. Then the ether was distilled off and the residue (0.025 g) was recrystallized from petroleum ether. This gave (V) with mp 111-112°C, R_f 0.86 [Al_2O_3, activity grade II, ethyl acetate–benzene (1 : 2) system]. A mixture of (V) with an authentic sample of pranferol acetate gave no depression of the melting point, and the IR spectra of the two substances coincided completely.

Acetylation of (VI). A mixture of 0.0064 g of (VI), 2 ml of acetic anhydride, and 0.5 ml of pyridine was heated for 1 h. Then it was cooled, diluted with water, and worked up in the usual way. Acicular crystals of (VII) (0.0055 g) deposited with mp 117-118°C (from petroleum ether), R_f 0.83 [Al_2O_3, activity grade II, ethyl acetate–benzene (1 : 2) system].

The IR spectra were taken on a UR-10 spectrometer (mulls in paraffin oil), the UV spectrum on an SF-4A spectrophotometer (solution in ethanol), the NMR spectra on a JNM-4H-100 spectrometer (solution in $CDCl_3$, internal standard TMS), and the mass spectra on a MKh-1303 instrument at an ionizing voltage of 30 V. The melting points were determined on a Kofler block.

SUMMARY

From the roots of Prangos ferulacea (L.) Lindl. has been isolated a new furocoumarin (I), $C_{10}H_{14}O_5$, with mp 136.5-138.5°C (from ethanol), $[\alpha]_D^{20}$ ± 0° (chloroform), which we have called gosferol.

On the basis of a study of the UV, IR, NMR, and mass spectra and the chemical properties of gosferol, the structure 5-(2"-hydroxy-3"-methylbutenyloxy)furo-2',3' : 7,6-coumarin has been proposed for it.

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