FUROCOUMARINS OF THE ROOTS OF Prangos ferulacea

A. Z. Abyshev, P. P. Denisenko,
N. P. Kostyuchenko, A. I. Ermakov,
and Yu. N. Sheinker

UDC 577.15/17:582.89

As is well-known [1-5], solutions of sulfuric acid or mixtures of glacial acetic and sulfuric acids are frequently used for cleaving alkoxylated coumarin compounds and the isomerization of their epoxy derivatives. This usually forms a mixture of a number of substances, since the reactions take place in several directions. Thus, for example, the treatment of natural oxypeucedanin (I) with 20% sulfuric acid in ethanol gives five substances, of which four compounds (II with mp 146-147°C, III with mp 135°C, IV with mp 136-138°C, and V) have been identified as, respectively, isooxypeucedanin, oxypeucedanin hydrate, gosferol, and bergaptol by mixed melting points of the substances obtained with authentic samples and by the similarity of their IR spectra. As can be seen, processes of isomerication, hydration, and the cleavage of an ether bond take place simultaneously. The properties of the fifth substance (VI), with mp 93-94.5°C did not correspond to any known coumarin derivative.

In the IR spectrum of (VI) there are two bands in the region of the stretching vibrations of carbonyl groups – at 1740 and 1710 cm^{-1}. One of these bands (1740 cm^{-1}) is due to the vibrations of a C=O group of an α-pyrone ring, and the second appears as a consequence of the splitting of the carbonyl band of the α-pyrone, since no splitting of the bands is observed in chloroform, where a single band remains at 1740 cm^{-1}, which excludes the possibility of the presence of a second C=O group in it. The spectrum also has absorption bands at (cm^{-1}) 3425 (hydroxy group), 1630, 1610, 1585, 1560 (aromatic ring), and 1380, 1350 (gem-dimethyl grouping).

The acetylation of (VI) with acetic anhydride in pyridine formed an acetyl derivative (VII) with mp 103-104°C, the IR spectrum of which lacked the absorption band of the hydroxy group. The ease of acetylation of (VI) shows the primary or secondary nature of the hydroxy group.

The NMR spectrum of (VI) (Fig. 1) has the following signals in the region of aliphatic protons: ethyl group at δ 1.10 ppm (triplet with an intensity of three proton units) and at δ 3.49 ppm (quartet of two proton units), the size of the chemical shift (CS) of the methylene group corresponding to the attachment of the latter to oxygen; methyl groups with δ 1.21 and 1.26 ppm (two singlets of three proton units each); a methine proton in a $-CH_2-CH-$ grouping at δ 3.93 ppm (multiplet in [D]acetone; quartet in CD_3OD, one proton unit);

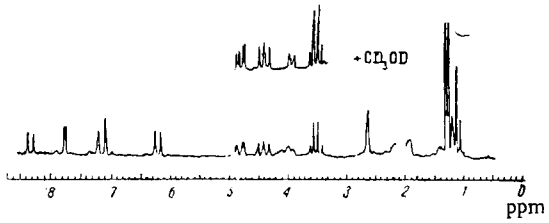


Fig. 1. NMR spectrum of substance (VI) solvent [D]acetone; internal standard TMS; JNM-4H-100 MHz.

Leningrad Sanitary and Hygienic Medical Institute. S. Ordzhonikidze All-Union Chemical and Pharmaceutical Scientific-Research Institute. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 45-49, January-February, 1972. Original article submitted July 8, 1971.

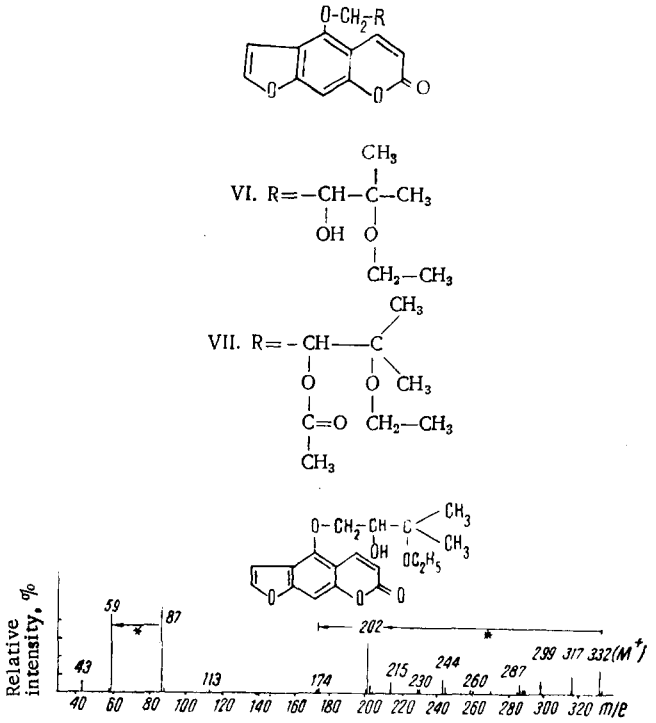
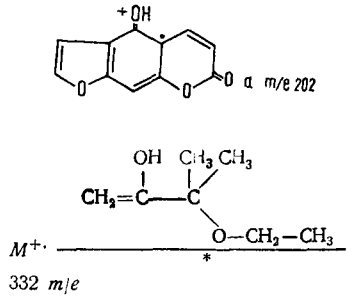


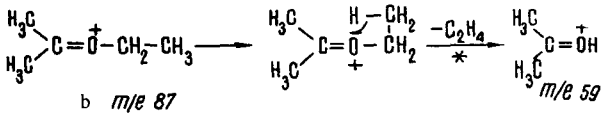
Fig. 2. Mass spectrum of substance (VI).

the protons of the $-CH_2$ group prove to be nonequivalent and appear in the spectrum in the form of two quartets with δ 4.37 and 4.83 ppm (with intensities of one proton unit each). The structure of the signals is determined by the two vicinal constants, $J_1 = 3$ Hz and $J_2 = 8$ Hz, and also by the geminal constant $J = 10$ Hz. A signal at δ 6.40 ppm (at 13°C) relates to the proton of a hydroxy group, and on heating to 70°C this signal shifts to 4.1 ppm. In the region of aromatic protons there are doublets with chemical shifts, δ, of 6.18, 8.29, 7.20, and 7.82 ppm due to the protons in positions 3 and 4 of the coumarin ring and the 4',5' protons of the furan ring, respectively. A singlet at δ 7.10 ppm is due to a proton in position 8. It follows from this that (VI) has the structure of 5-(3"-ethoxy-2"-hydroxy-3"-methylbutoxy)furo-2',3' : 7,6-coumarin.

The proposed structure of (VI) agrees well with the mass spectrum (Fig. 2) in which the molecular ion M^+ 332 m/e clearly appears. As for the decomposition of gosferol and its acetate, the characteristic direction of the fragmentation of (VI) is the formation of structure *a* with the migration of a hydrogen atom to the charged oxygen atom (first direction).



The second direction of decomposition is the formation of a stable electron-saturated fragment b, and therefore this process is energetically more favorable than the process corresponding to the appearance of structure *a*. The peak of the fragment b with m/e 87 is the maximum peak in the spectrum.



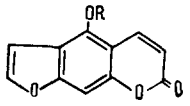
The structure of fragment b is also shown by a further decomposition, confirmed by a metastable peak. The peak of fragment c with m/e 59 is also one of the maximum peaks in the spectrum.

Thus, in the treatment of (I) with 20% sulfuric acid in ethanol, in addition to the reactions described above [1-5], the ethoxylation of the tertiary hydroxy group in the side chain takes place, leading to compound (VI).

From the biogenetic point of view the formation of substance (IV) (gosferol) under these conditions is interesting since it is the second furocoumarin that we have recently isolated from the roots of Prangos ferulacea containing only one hydroxy group in the side chain. In addition to other furocoumarins (I, III), gosferol (IV) and pranferol (VIII) were isolated from the roots of one and the same plant, and therefore it may be assumed that (IV) is a precursor of (VIII) in the plant organism. In its turn, (IV) is apparently formed from (III) by dehydration. In actual fact, when (III) was treated under the same conditions as (I) we obtained (II, IV, V, and VI), which were identified by mixed melting points with authentic samples and by the similarity of their IR spectra, which is in harmony with our hypothesis.

Thus, on the basis of the facts presented and the closeness of the structures of the furocoumarins isolated it may be assumed that their formation in the roots of Prangos ferulacea takes place by related biosynthetic mechanisms.

Since the plant studied contains a furocoumarin from the isopentyl group – isoimperatorin (IX) – apparently formed by the alkylation of bergaptol (V),* it is natural to assume that this group represents the initial stage in the formation of the side chain of the furocoumarins after which follow epoxidation, hydroxylation, dehydration, and hydrogenation.



V. R=H

IX. $R=CH_2-CHC=C(CH_3)(CH_3)$

I. $R=CH_2-CH-C(O)(CH_3)(CH_3)$

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

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

VIII. $R=CH_2-CH(OH)-CH(CH_3)(CH_3)$

SUMMARY

It has been established that the treatment of oxypeucedanin and oxypeucedanin hydrate with 20% sulfuric acid in ethanol forms, in addition to known substances, a new coumarin derivative (VI), $C_{18}H_{20}O_6$, with mp 93-94.5°C, for which the structure of 5-(3"-ethoxy-2"-hydroxy-3"methylbutoxy)furo-2',3' : 7,6-coumarin has been proposed. On the basis of the investigation performed and the similarity of the structures of the compounds isolated, a hypothetical scheme of the biogenesis of furocoumarins in Prangos ferulacea (L.) Lindl. has been put forward.

* We did not isolate bergaptol, but the presence of this compound in an extract was detected chromatographically.

LITERATURE CITED

1. G. A. Kuznetsova, A. Z. Abyshev, M. E. Perel'son, Yu. N. Sheinker, and G. Yu. Pek, Khim. Prirodn. Soedin., 2, 310 (1966).
2. J. F. Fisher and H. E. Nordby, Tetrahedron, 22, No. 4, 1489 (1966).
3. C. R. Ghoshol, S. S. Gupta, and A. Chatterjee, Chem. and Ind. (London), 1963, No. 34, 1430.
4. E. Spath and K. Klager, Ber., 72, 920 (1933).
5. P. W. Chow, A. M. Duffield, and P. R. Jefferies, Aust. J. Chem., 19, No. 3, 483 (1966).