STRUCTURE OF THE PRODUCT OF THE SENSITIZED PHOTODIMERIZATION OF PEUCEDANIN

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It is known that natural coumarins and furocoumarins are capable of changing in two directions under the action of light, undergoing either photodimerization or cis-trans isomerization at the double bond of the pyrone ring with the formation of analogs of coumaric acids. The study of the structure of the compounds obtained in this way presents undoubted interest, since the biological and, in particular, therapeutic activity of many coumarins appears only when they have been irradiated with ultraviolet light or x rays (treatment of vitiligo, malignant neoplasms, etc.).

On considering the products of the irradiation of herniarin (I) and other compounds, Wesseli et al. [1-3] came to the conclusion that they are bimolecular compounds formed through the double bond of the α-pyrone ring with the appearance of a so-called cyclobutane structure (Ia).

It was assumed at first that coumarins and furocoumarins of the angular type tended to undergo photodimerization, while furocoumarins with a linear linkage of the rings did not take part in this reaction. However, a capacity for photodimerization was soon [4] noted in psoralen, xanthotoxin, bergapten, and a whole series of other furocoumarins of the linear series. These compounds were found not only to form dimers but also analogs of furocoumarinic acid (II). A consideration of the UV spectra of the furocoumarin dimers obtained showed that their structure differed from that of the dimers of the simplest coumarins. All coumarin derivatives have an absorption band in the 295-330 nm region due to the conjugation of the π electrons of the aromatic nucleus and of the double bond and the carbonyl of the α-pyrone. The absorption of the furan ring in this region is insignificant. In the formation of dimers through the double bond of the pyrone ring, the absorption maximum in this region should disappear, which is not in fact observed. On this basis, Lerner (cited in [5, 6]) put forward the hypothesis that the formation of furocoumarin dimers involved the double bonds of the furan ring of one and of the lactone ring of the other molecule. Nothing at all was known about dimers of compounds with a substituted furan nucleus.

We have previously reported that in the benzophenone-sensitized photodimerization of the natural furocoumarin peucedanin, a mixture of at least five substances is formed [7]. Using spectral methods, we have continued a study of one of the main products of the reaction, with the composition $C_{21}H_{20}O_6$ and mp 234-235°C. (See Scheme on following page.)

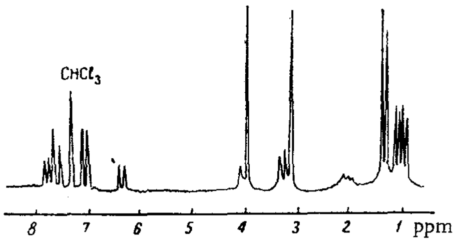

Fig. 1. NMR spectrom of the photodimer of peucedanin.

The mass spectrum of the substance has peaks with m/e 488 and 472, corresponding to the fragments arising by the injection of CO and CO_2 from the coumarin molecule. Thus, although because of its instability the substance did not give a molecular peak, its molecular weight must, taking the nature of the fragmentation of coumarins under the influence of electron impact into account, be 516 proton units. These results show that the lactone under investigation is a dimer of peucedanin and has the composition $C_{30}H_{28}O_8$.

In its NMR spectrum (solution of the substance in $CDCl_3$), there are two doublets with δ 7.70 and 6.26 ppm, J = 9.5 Hz, due

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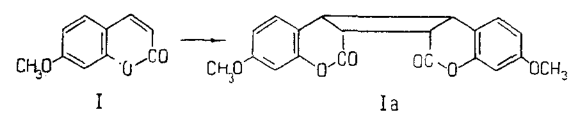
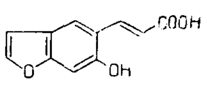
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodynkh Soedinenii, No. 6, pp. 680-683, November-December, 1970. Original article submitted October 19, 1970.



I Ia



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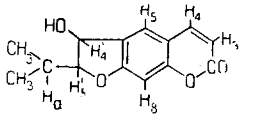

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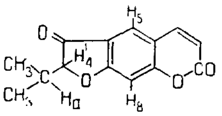

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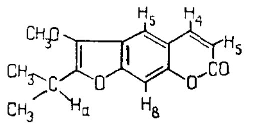

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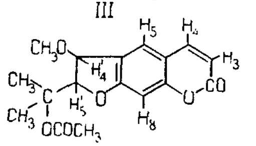

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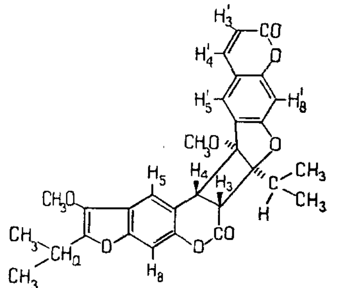
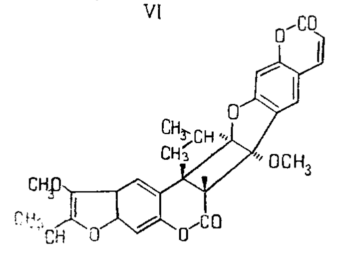


VII



VIII

to the two H-4 and H-3 interacting protons. Their intensity of 1 H each shows the presence in the molecule of the dimer of one α, β-unsaturated lactone ring. Four singlets at 7.58 and 6.91 and at 7.45 and 7.02 ppm are due to the presence of four aromatic protons – H-5 and H-8 of one and H-5' and H-8' of the other benzene ring. Judging from the δ values of the corresponding protons of dihydrooreoselol (III), oreoselol (IV), and peucedanin (V), it may be assumed that in substance VI the first two signals are due to the H-5' and H-8' protons of the benzodihydrofuran nucleus and the other two to the H-5 and H-8 protons of the benzofuran nucleus [8]. Singlets at 3.93 and 3.09 ppm (3 H each) are due to the presence of two methoxy groups, one of which (3.93 ppm) is in the $C_{4'}$ position of a furan ring and the other at $C_{4'}$ of a dihydrofuran ring. Doublets at 4.05 ppm (partially superposed on a singlet at 3.99 ppm) and 3.29 ppm, J = 10 Hz, with an intensity of 1 H each are caused by two interacting protons in a $\mathrm{Ar{-}\underset{|}{C}H{-}\underset{|}{C}H{-}CO}$ grouping and are assigned to a substitute dihydropyrone ring (dihydrocoumarin). Furthermore, the NMR spectrum has two multiplets (1 H each), one of which, superposed on the doublet at 3.29 ppm, corresponds to the methine proton of an isopropyl grouping at $C_{5'}$ of a furan ring and the other, at 1.90-2.20 ppm to the analogous proton at $C_{5'}$ of a dihydrofuran ring. The diamagnetic shift of the second signal is apparently due to the anisotropic influence of the carbonyl of the dihydropyran ring. Two singlets at 1.29 and 1.35 ppm and also doublets at 1.06 and 0.95 ppm, J = 6.5 Hz (3 H each) are due to the protons of $(CH_3)_2C$ groups at $C_{5'}$ of a furan and a dihydrofuran ring [8]. Consequently, the substance under investigation is a dimer of peucedanin formed at the expense of the double bonds of α-pyrone and furan rings in the "head to tail" manner and has one of the most probable structures VII and VIII. The structure proposed fully explains the physicochemical properties of the dimer. Its IR spectrum has two carbonyl absorption bands, one of which, at 1733 cm^{-1}, corresponds to an $\alpha,\beta,\gamma,\delta$-unsaturated lactone ring and the second, at 1758 cm^{-1}, to a γ, δ-unsaturated lactone ring. The presence of the latter imparts to the compound the properties characteristic for dihydrocoumarins – ease of opening of the lactone ring on boiling with water and under the action of weak alkalis with the formation of a hydroxy acid, the production of ether-esters on alkylation, etc.

G. O. Schenk [9] and Hammond et al. [10], studying the photodimerization of coumarin, found that the order of addition of the molecules to the dimer and the configuration at the asymmetric centers depend on the conditions of performing the reaction. Thus, in the nonsensitized dimerization of the substance in ethanolic solution or of a suspension in water a cis isomer of the "head to head" type is formed. Irradiating benzene solutions in the presence of benzophenone or β-carotene as sensitizer leads to the appearance of two trans isomers of the "head to head" and "head to tail" types. The question of the order of coupling of the molecules in the peucedanin dimer requires further study. In view of the above-mentioned diamagnetic shift of the signal of the methine proton, structure VII must be considered the most likely.

The NMR spectra of the dimer and of dihydrooreoselol were taken on a JNM-4H-100/100 MHz spectrometer in deuterochloroform, and the δ values of the other substances were taken from the literature [8].

TABLE 1. Characteristics of the NMR Spectra

Substance	Chemical shifts								
	H-3	H-4	H-5	H-8	CH_3	H_a	H_4'	H_5'	OCH_3
III	6,23 d (J=10 Hz)	7,66 d (J=10Hz)	7,58 s	6,80 s	1,21 1,28 s	2,4-2,8 m	5,25 d (J=6 Hz)	4,12 q (J= 6 Hz)	—
IV	6,33 d (J=10Hz)	7,69 d (J=10 Hz)	7,80 s	7,01 s	0,86 1,18 d (J=6,7 Hz)	1,66 dd (J=4, 5, 6, 7 Hz)		4,53 d (J=4,5 Hz)	—
V	6,44 d (J=10Hz)	7,88 d (J=10 Hz)	7,64 s	7,35 s	1,44 d (J=7,1 Hz)	3,33 m	—	—	4,02 s
VI	6,16 d (J=10Hz)	7,56 d (J=10 Hz)	7,38 s	6,71 s	1,42 1,60 d	—	4,98 d (J=2,4 Hz)	4,78 d (J=2,4 Hz)	3,41

Note: s) singlet; d) doublet; m) multiplet; q) quartet.

SUMMARY

On the basis of the NMR spectrum, a most probable structure has been proposed for the product of the sensitized photodimerization of the natural furocoumarin peucedanin. It has been shown that the latter is formed at the expense of the double bonds of the α-pyrone ring of one and of the furan ring of the second molecule in the "head to tail" manner.

LITERATURE CITED

1. F. Wesseli and F. Kallab, Monatsh., 59, 161, 1932.
2. F. Wesseli and K. Dirjaski, Monatsh., 64, 131, 1934.
3. F. Wesseli and I. Plaichinger, Ber., 971, 75, 1942.
4. F. Wesseli and I. Kotlan, Monatsh., 86, 430 (1955).
5. W. L. Fowlks, J. Invest. Dermatol., 32, No. 2, 2, 249, 1959.
6. G. Rodighiero and V. Cappellina, Gass. Chim. Ital., 91, No. 1, 103, 1961.
7. G. K. Nikonov, ZhOKh, 34, 2815, 1964.
8. M. E. Perel'son, Yu. N. Shenker, G. P. Syrova, G. K. Nikonov, and A. P. Prokopenko, "The use of NMR spectroscopy in the chemistry of natural coumarins," in: Medicinal Plants [in Russian], Vol. 15, Moscow, 1969, p. 60.
9. G. O. Schenk, I. Wilucki, and C. H. Krauch. Ber., 95, 1409, 1962.
10. G. S. Hammond, Ch. A. Stout, and A. A. Lamola, J. Am. Chem. Soc., 86, No. 15, 3103, 1964.