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THE STRUCTURE OF PEUCENOL (PEUMORISIN)—A NEW HYDROXYCOUMARIN

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In the chemical study of the substances isolated from the roots of Peucedanum morisonii Bess, G. K. Nikonov and I. A. Ivashenko [1] obtained and characterized for the first time a new hydroxycoumarin $C_{20}H_{24}O_3$ which they called peucenol. Independently, the same hydroxycoumarin was isolated and studied by V. I. Zaretskii, N. S. Vul'fson, L. S. Chetverikova, and V. G. Zaikin [2], who gave it the name peumorisin. From the elementary analysis and a mass spectrometric determination of the molecular weight, these authors found the true empirical formula for this compound, $C_{19}H_{22}O_3$.

They established the structure of the compound isolated by fragment mass spectrometry [2]. It was concluded that the most probable structure for peumorisin was 7-hydroxy-8-(3-methylene-7-methyloct-6-en-1-yl)coumarin.

Continuing a study of the structure of this coumarin using NMR spectra, we have found that the proposed structure is not in harmony with the NMR spectrum of the compound under consideration (in this paper it is called peucenol).

In the first place, the NMR spectrum of peucenol shows a different arrangement of the substituents in the coumarin nucleus. The signals in the 6-8 ppm region (Fig. 1a) show that in addition to the quadruplet from the protons in positions 3 and 4 [3], there are two other signals in this region (7.06 and 7.14 ppm) with intensities corresponding to one proton unit each. This nature of the signals in this region unambiguously shows the presence in the molecule of protons in positions 5 and 8 and substitution in positions 6 and 7 [3].

On the basis of the biogenesis of the coumarins and the UV spectra in neutral and alkaline media [2,4] it may be concluded that there is a hydroxy group in position 7. Hence, the second substituent, with the over-all formula $C_{10}H_{17}$ must be at position 6. Consequently, peucenol is an isomer of ostruthin.

The substituent in position 6 cannot consist of a chain of two combined dimethylallyl links, as was suggested previously [2], since the NMR spectrum of peucenol lacks signals in the 4.5-6 ppm region characteristic for protons on C=C double bonds.

In considering the sequence of signals in the spectrum relating to this substituent, one must first of all take into account the strong single peak at 0.94 ppm (6 proton units) which undoubtedly relates to two methyl groups attached to

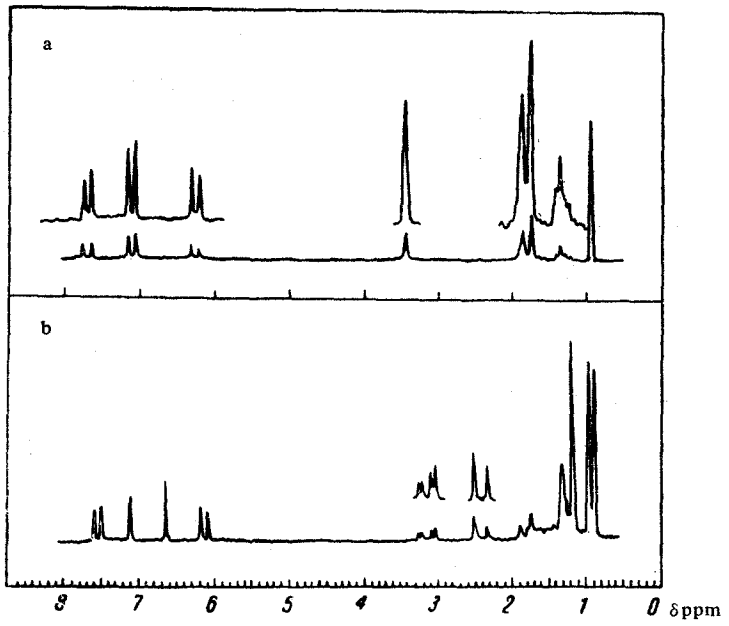


Fig. 1. NMR spectra of peucenol (a) and the product of its cyclization (b) in deuteriochloroform (O-tetramethylsilane).

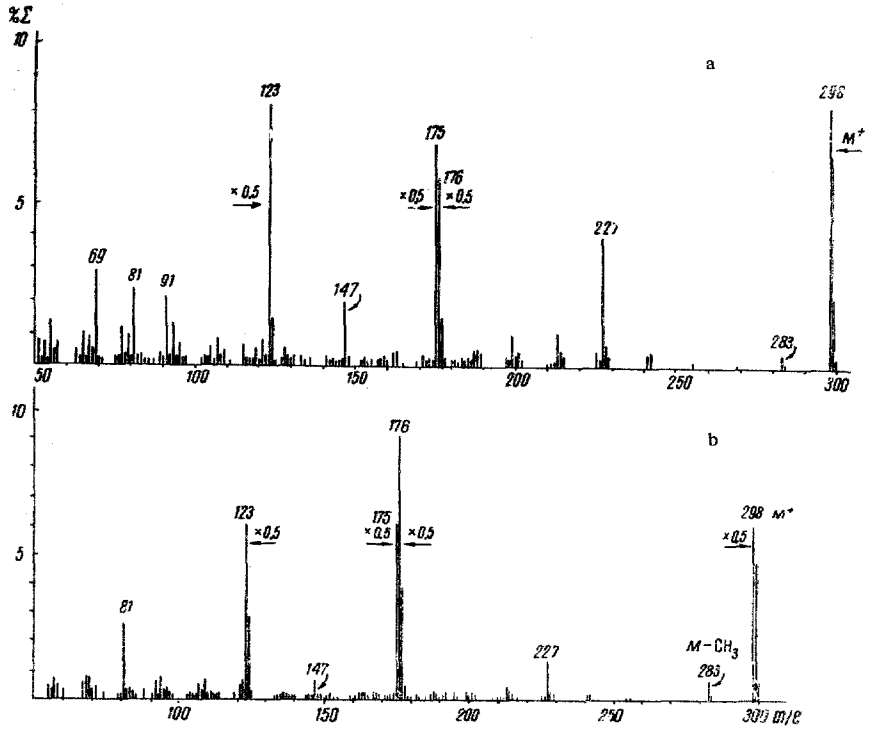
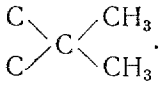
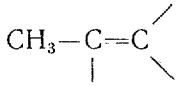
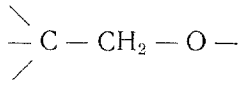


Fig. 2. Mass spectra of peucenol (a) and the product of its cyclization (b).

a saturated quaternary carbon atom, most probably the fragment

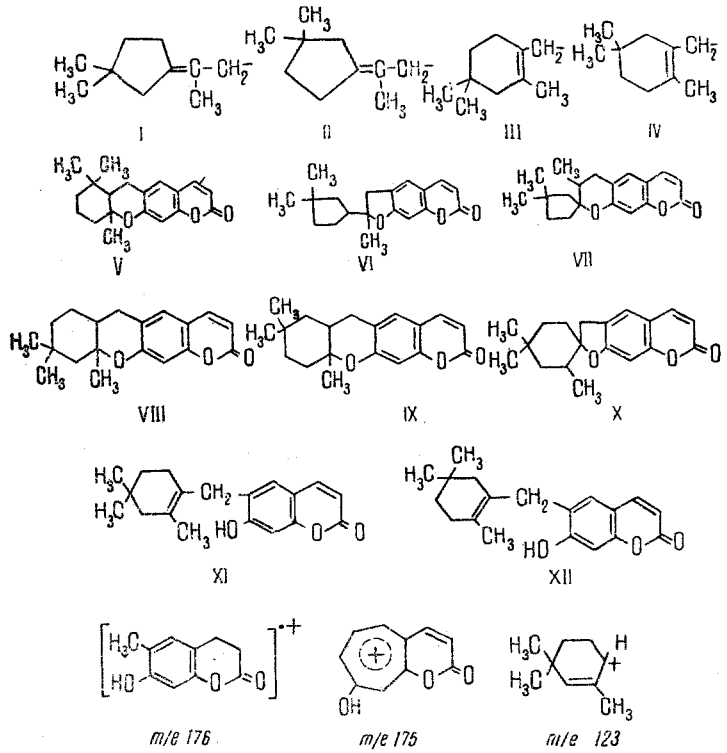


Another somewhat broadened signal with an intensity of 3 proton units is observed at 1.75 ppm; it is apparently due to a CH_3 group on a double bond  . Since the spectrum contains no signals of protons on a double bond, it is obvious that the remaining valences of the C=C group are satisfied by carbon atoms. One of these substituting groups must be a CH_2 group also attached to the coumarin nucleus. This follows from the presence in the spectrum of a single signal with an intensity of two proton units at 3.44 ppm. Another possible variant of the fragment for this signal,  , is excluded because of the basence of an oxygen atom from the side chain. The remaining two positions on the double bond are likewise occupied by two CH_2 groups, but these groups are then connected with saturated carbon atoms (broadened signal at 1.88 ppm with an intensity of 4 proton units). Finally, the broadened signal with an intensity of 2 proton units at 1.37 ppm corresponds to a CH_2 group present in an environment of saturated carbon atoms. Its splitting is due to spin-spin coupling with one of the CH_2 groups attached to the double bond, as is confirmed by double resonance.

On the basis of all the results obtained, the four possible structures I–IV may be proposed for the substituent in position 6.

It must be observed that the structures suggested do not correspond to the isoprene rule.

The possible variants of the structure of peucenol permitted the expectation that it would undergo Späth cyclization [5]. In actual fact, when it was heated with hydrobromic acid an isomeric product with mp 202–202.5° C was isolated the IR spectrum of which lacked the band of a hydroxyl group. Judging from the melting point, it differed from the products obtained by Späth in the cyclization of ostruthin and, in particular, from substance A with mp 181–182° C, to which structure V was ascribed [5, 6].



A study of the NMR spectrum of the product of the cyclization of peucenol (Fig. 1) permits structures I and II to be excluded from consideration. In actual fact, the cyclization of the compound with structure I, for example, would be expected to lead to the formation of products VI and VII. In the first of them the protons of the methylene group attached to the aromatic ring can interact with one another, and in the second the splitting of the signal of one of the methyl groups must take place. In the spectrum of the compound obtained (Fig. 1b) the methylene group forms a quartet at 3.21 ppm (J_1 = 6.5 Hz; J_2 = 18 Hz) and a doublet at 2.43 ppm (J = 18 Hz). Thus, the methylene group is probably attached to the ring; the two protons are nonequivalent and interact with one another. At the same time, one of the protons of the methylene group also reacts with one proton on the neighboring carbon atom. For this reason, the spectrum does not correspond to structure VI. Furthermore, the cyclization product cannot have structure VII, either, since no splitting of the signal of one of the three methyl groups is observed. From the same considerations, the structure of peucenol cannot be described by means of the formula II.

Structures VIII and IX, corresponding to III and IV, on the other hand, are in full agreement with the observed spectrum. The shift of the signals of the methylene and one of the methyl groups into the strong field correspond to the disappearance of the double bond; at the same time, the position of the methyl singlet at 1.20 ppm corresponds to a methyl group of the type of $CH_3-\overset{|}{\underset{|}{C}}-C-Ar$.

The formation of compounds of type X on cyclization must be excluded, as in the case of VII, because of the absence of splitting of the signal of one of the methyl groups.

From what has been said, formulas XI and XII can be put forward as the most probable for peucenol.

An additional mass spectrometric investigation using a system for the introduction of the sample directly into the ion source ("direct introduction of the sample") showed that the mass spectrum of peucenol obtained under these conditions differs somewhat from the spectrum of this compound recorded earlier in an instrument with a metal flask inlet [2]. Actually, in the "direct introduction" spectrum (Fig. 2a) the peaks M − 2H and M − 4H are absent, and so are the peaks of fragments due to the dehydrogenation of the sample in the inlet flask before electron impact. At the same time, the relative intensities of the molecular peak (m/e 298) and the peaks with m/e 175, 176, and 123, due to the elimination of the carbocyclic link, rise considerably. For comparison, we also recorded the spectrum of ostruthin. It was found that the decomposition of the latter under electron impact differs substantially from the fragmentation of peucenol.

The mass spectrum of the cyclization product (Fig. 2b) is extremely similar to that of peucenol and differs from the latter mainly by the relative intensities of the peaks of the main characteristic fragments: M^+, m/e 298; M − 122, m/e 176, M − 123, m/e 175; m/e 123.

The similarity of the mass spectra of peucenol and the product of its cyclization (VIII or IX) permits the assumption that the mechanism of the decomposition of these compounds is similar, on the whole. This is also confirmed by the fact that the mass spectra of peucenol and VIII or IX retain the metastable peaks of similar mass number corresponding to the following transitions: $M^+ \rightarrow$ 176 (104; calc. 103.9); $M^+ \rightarrow$ 123 (51; calc. 50.7); 123 $\rightarrow$ 81 (53.3; calc. 53.2). Thus, these spectra do not permit a choice between formulas XI and XII (for peucenol) and between VIII and IX for the product of its cyclization.

Experimental

The PMR spectra were taken on a JNM-4H-100 spectrometer, the IR spectra on a UR-10 spectrometer, and the mass spectra of a MKh-1303 instrument fitted with a system for the introduction of the sample directly into the ion source [7] at 120–150° C with an ionization voltage of 70 V.

Cyclization of peucenol. A solution of 1.91 g of the substance in 20 ml of conc hydrobromic acid was treated with 0.2 g of red phosphorus and the mixture was boiled for 1 hr. The liquid was diluted with 200 ml of water and treated with ether (5 × 50 ml). The ethereal extracts were combined, washed with 0.5% caustic potash solution, and evaporated to dryness. Colorless crystals with mp 202–202.5° C (from methanol) were obtained. Yield 0.5 g.

Found, %: C 76.63; 76.67; H 7.75; 7.37. Calculated for $C_{19}H_{22}O_3$, %: C 76.71; H 7.38.

Conclusions

On the basis of a spectroscopic study of peucenol (peumorisin) and the product of its cyclization, it has been established that peucenol is either 7-hydroxy-6-(2',4',4'-trimethylcyclohex-1-enylmethyl)coumarin or 7-hydroxy-6-(2',5',5'-trimethylcyclohex-1-enylmethyl)coumarin.

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