THE STRUCTURE OF THE PRODUCTS OF TRANSFORMATION OF SUBEROSIN AND THEIR POSSIBLE BIOGENESIS

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In an investigation of the coumarin composition of Prangos lophoptera Boiss., together with other compounds we isolated a substance (I) with the composition $C_{15}H_{16}O_3$, mp 85-86.5°C, which was shown to be identical with the known coumarin suberosin [1, 2]. The latter has not previously been found in plants of the genus Prangos. Subsequently, in work with this compound it was found that when a chloroform solution of (I) was allowed to stand in the light at room temperature at least three substances (II, III, and IV) were formed, the main and final product of the photoreaction being compound (III). It appeared of interest to determine the route for the formation of these components and to study their structure, since the authors who investigated the structure of (I) previously [1-4] did not observe such a process.

In order to obtain each of the compounds formed in sufficient amount and to determine their nature, a sample of (I) was dissolved in chloroform and the solution was left in an illuminated place at room temperature. The course of the photoreaction was monitored by chromatography in a thin layer of absorbent beginning from the moment of dissolution of the (I) in the solvent and continuing until the reaction ceased. During the first 3-5 h, the main product was (II) with traces of (III) and (IV). After 6-10 h, the concentration of (III) in the solution had increased and that of (II) had decreased. Finally, after a day and more only traces of (II) and (IV) were found in the solution, and the main component of the photoreaction had become (III). Thus, as a result we obtained in the individual state substances (II) with the composition $C_{15}H_{16}O_4$, mp 172-174°C, and (III) with the composition $C_{15}H_{16}O_5$, mp 184-185°C, M^+ 276. It has not yet been possible to obtain substance (IV) in the crystalline state, since its amount in the reaction mixture is very small.

The NMR spectrum permitted the conclusion that (II) has the structure of 6-(3'-hydroxyisopent-1'-en-1'-yl)-7-methoxycoumarin, corresponding to the known coumarin suberenol (V) isolated previously from the bark of Xanthoxylum dominianum Merr. and Parry (Rutaceae) [5]. The identity of (II) and (V) was shown by the preparation of 7-methoxycoumarin-6-carboxylic acid (VI), $C_{11}H_8O_5$, mp 261-262°C (from ethanol) when (II) was oxidized with chromium trioxide in glacial acetic acid, and also by the similarity of the NMR spectra of (II) and natural suberenol.

The results of an analysis of the NMR and mass spectra of (III) showed that the latter is 6-(3'-hydroxy-1',2'-epoxyisopentyl)-7-methoxycoumarin (lophopterol), as was confirmed by the absence of a depression of the melting point of a mixture of (III) with natural lophopterol.

The facts given above show that when a chloroform solution of (I) is allowed to stand at room temperature with the access of atmospheric oxygen, oxidation of the double bond in the side chain and the migration of hydrogen from the methylene group attached to the aromatic ring take place with the formation of a hydroxy group on the quaternary carbon atom (formation of trans-suberenol). A conjugated double bond is created in the side chain which is also oxidized, giving an epoxy group (formation of lophopterol) (see scheme on next page).

Oxidation by atmospheric oxygen in chloroform solutions at room temperature has also been observed in work with mammein (VII) [6] and colupenol (VIII) [7]. No such oxidation takes place with an isomer of (I) – 8-(isopent-2'-en-1'-yl)-7-methoxycoumarin (osthole) (IX), as has been established experimentally under similar conditions.

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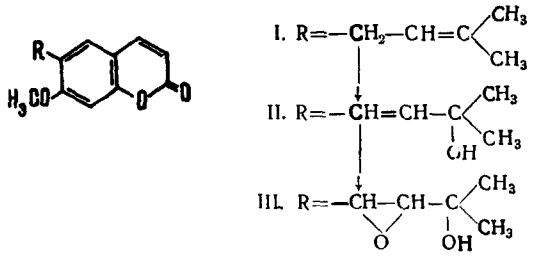
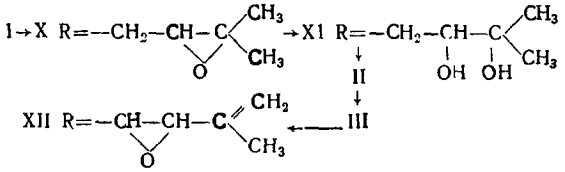


VI. R=—COOH Scheme

Since we isolated (II) and (III) from chloroform extracts of the fruit and stems of Prangos lophoptera Boiss., in which (I) is also present, the question arose as to whether these compounds are metabolites of (I) formed during the standing of the extract at room temperature. This question was answered unambiguously by the results of a study of fresh chloroform extracts from the roots, fruit, and stems by thin-layer chromatography using authentic samples of (II) and (III). It was established that of the substances mentioned the roots contain only (I), in addition to other coumarin derivatives, while the fruit and stems contain all three compounds (I, II, and III). This shows that (II) and (III) are natural components of the fruit and stems of Prangos lophoptera that are formed by biosynthesis in the plant organism:



Substance (X) and the related substances (XI) and (XII) have not yet been found in P. lophoptera. However, we have found analogs of them in other species of the genus investigated: Merancin (XIII) and merancin hydrate (XIV) have been found in the roots of Prangos ferulacea (L.), and ulopterol (XI) has been isolated from the roots and fruit of Prangos uloptera DC. [8-11]. Consequently, it is not excluded that these components also exist in the plant studied, which contains their precursors (I) and (IX), but the amounts of these compounds are so small that it has not been possible to isolate sufficient of them for a more detailed investigation.

EXPERIMENTAL METHOD

The NMR spectra were taken on a Varian HA-100D spectrometer in $CDCl_3$; 0 — HMDS; and the mass spectra were taken on a LKB-9000 instrument. The melting points were determined on a Kofler block. Thin-layer chromatography (TLC) was carried out on a nonfixed layer of alumina (activity grade IV) in the ethyl acetate—benzene (1 : 4) and chloroform systems. The amounts of substances formed in the reaction mixture were estimated from the areas of the spots on chromatograms.

Preparation of (II). A solution of 0.75 g of (I) in 30 ml of chloroform was left in an illuminated place at room temperature. After 4 h, the solvent was evaporated off and the residue was separated by preparative TLC. This gave 0.22 g of (II), $C_{15}H_{16}O_4$, mp 172-174°C (from petroleum ether), which was shown to be identical with natural suberenol from the absence of a melting point of a mixture with the authentic material and from the similarity of their NMR spectra.

Oxidation of (II). A solution of 0.4 g of chromium trioxide in 10 ml of 50% glacial acetic acid was added to a solution of 0.2 g of (II) in 10 ml of glacial acetic acid, and the mixture was left at room temperature. After a day, it was diluted with water and extracted with ether. The usual working up gave about 0.11 g of crystalline substance (VI), $C_{11}H_8O_5$, mp 261-262°C (from ethanol), corresponding by its melting point to 7-methoxycoumarin-6-carboxylic acid.

Preparation of (III). The residue from the reaction mixture (0.5 g) after the isolation of (II) was dissolved in 20 ml of chloroform and was left under the same conditions for 24 h. Then the solvent was evaporated off on the water bath, and the residue was separated by preparative TLC. This gave (III), $C_{15}H_{16}O_5$, mp 184-185°C [from chloroform—petroleum ether (1 : 2)]. A mixture of (III) with a sample of natural lophopterol showed no depression of the melting point.

Attempted Oxidation of (IX). A solution of 1.0 g of (IX) in 50 ml of chloroform was left at room temperature. The course of the reaction was monitored by the TLC method. Over a month no changes whatever took place in the (IX). Then the solvent was evaporated. The initial substance with mp 82-83°C, identical with osthole (IX) was recovered.

SUMMARY

When suberosin is allowed to stand in chloroform at room temperature with access of atmospheric oxygen, photooxidation takes place with the formation of at least three substances: (II), $C_{15}H_{16}O_4$, mp 172-174°C; (III), $C_{15}H_{16}O_5$, mp 184-185°C; and (IV).

It has been established by NMR and mass spectroscopy and also by their chemical properties, that (II) is 6-(3'-hydroxyisopent-2'-en-1'-yl)-7-methoxycoumarin (trans-suberenol) and (III) is 6-(1',2'-epoxy-3'-hydroxyisopentyl)-7-methoxycoumarin (lophopterol). The nature of (IV) has not yet been determined.

It has been shown experimentally that no such oxidation takes place with an isomer of (I) – osthole (IX). A scheme for the biogenesis of coumarins in the organism of the plant investigated has been put forward.

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