STRUCTURE OF SOME COMPONENTS OF THE ROOTS OF *Prangos ferulacea*

A. Z. Abyshev

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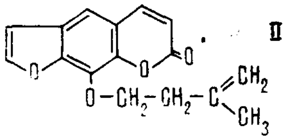
The isolation of four coumarin compounds (I-IV) from a methanolic extract of the roots of *Prangos ferulacea* growing in the Nakhichevan ASSR (Shakhbuz), one of which was identified as meransin hydrate (I), found for the first time in nature, has been reported previously [1]. In a further investigation of this extract, another two substances – (V) and (VI) – of coumarin nature have been isolated. The present paper gives the results of a study of the structure of compounds (II-VI) and of two other components (VII and VIII) isolated from the roots of the plant under investigation collected in Armenia (Sisian). Substances (III-VI) have also been detected in other Caucasian species of the genus *Prangos* (in the roots and fruit of *Prangos uloptera*, in the roots of *Prangos alata*, and in the roots and fruit of *Prangos lophoptera*).

Substance (II), with the composition $C_{16}H_{14}O_4$, mp 119-120°C, M^+ 270, possesses a yellow fluorescence in UV light and belongs to the linear 8-monosubstituted furocoumarins, as follows from its IR and NMR spectra.

The IR spectrum of (II) shows absorption bands at 1725 cm^{-1} (α-pyrone C = O), 1608 cm^{-1} with an inflection at 1630 (C = C bond in an aromatic ring), 1210 cm^{-1} (ether bond), and 820 cm^{-1} (furan ring).

When (II) was treated with a mixture of sulfuric and acetic acids, a known furocoumarin was formed – xanthotoxol, $C_{11}H_6O_4$ (IX), mp 250-251°C (decomp.) – showing that (II) is an 8-hydroxypsoralen derivative and has a side chain consisting of C_5H_9. To confirm the structure of (II) and to interpret the side chain, we used the NMR spectrum, which contains the signals of the protons of a methyl group on a double bond (1.67 ppm, singlet, 3H) and those of three methylene groups, one of which is present on a double bond (4.80 and 4.92 ppm, singlets, 1H each), a multiplet at 3.72 ppm (2H) and singlets at 1.76 and 1.84 ppm (1H each) due to an $O-CH_2-CH_2$ grouping. In the region of aromatic protons there are doublets at 6.12 and 8.20 ppm (J = 9.5 Hz) and 6.95 and 7.65 ppm (J = 2.5 Hz) due to the protons in positions 3 and 4 of the coumarin nucleus and positions 4' and 5' of the furan ring, respectively. A singlet at 7.42 ppm relates to a proton in position 5. The facts given permit the proposal for (II) of the structure of 8-(3''-methylbutenyloxy)furo-2',3': 7,6-coumarin, which we have called feruliden.



II

Substances (III), $C_{19}H_{22}O_6$, and (IV), $C_{20}H_{24}O_6$, are apparently liquids, since attempts to crystallize them from various solvents proved unsuccessful. These compounds possess a bright-blue fluorescence in UV light and belong to the group of phenolic coumarins: the reaction with a 5% solution of ferric chloride was positive. When (III) and (IV) were treated with alkali, their R_f values changed, which showed the presence of an ester bond in the molecule of these compounds.

The IR spectrum of (III) showed absorption bands at 3300 cm^{-1} (hydroxy group), 1710-1730 cm^{-1} (C = O groups of an α-pyrone and of an ester), 1615 and 1510 cm^{-1} (aromatic nucleus), and 1410 and 1390 cm^{-1} (gem-dimethyl grouping).

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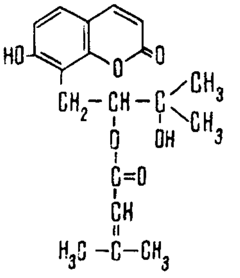
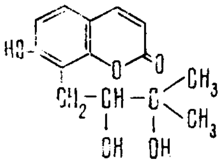
In the NMR spectrum of (III), three-proton singlets were observed in the strong field at 1.27, 1.30, 1.65, and 1.81 ppm due to the protons of a gem-dimethyl grouping and of methyl groups in an acid residue. A signal at 2.29 ppm (1H) is due to the proton of an alcoholic hydroxy group. A doublet at 3.55 ppm (2H, J = 8 Hz) belongs to the protons of a methylene group attached to an aromatic nucleus, and a broadened signal at 5.03 ppm (2H) is possibly due to the proton of a phenolic hydroxy group and to a geminal proton at an ester group. A one-proton signal with its center at 5.26 ppm probably belongs to an olefinic proton in an acid residue. In the weak-field region, four doublets are observed with chemical shifts of 6.17, 7.57 ppm (J = 10 Hz) and 7.14, 6.85 ppm (J = 9.5 Hz), corresponding to the protons in positions 3, 4, 5, and 6 of a coumarin nucleus.

On the basis of its IR and NMR spectra, substance (III) has been called ferudiol; it can be assigned to the 7,8-disubstituted coumarins, and the structure of 7-hydroxy-8-(3'-hydroxy-2'-senecioyloxyisopentyl) coumarins may be proposed for it.



III

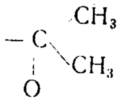
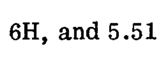
Such a structure agrees completely with the results of a study of the products of saponification of (III) with 10% KOH in methanol. This led to the formation of senecioic acid (X) with mp 67-69°C and an oily substance (XI), the methylation with dimethyl sulfate in alkali of which led to meransin hydrate (XII) with mp 126-127°C, showing that (XI) is 8-(2',3'-dihydroxyisopentyl)-7-hydroxycoumarin.

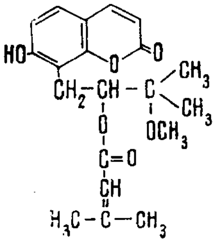


XI

The IR and NMR spectra of (IV) almost coincide with the spectra of (III), which enables it to be assigned to the 7,8-disubstituted coumarins, as well.

In the IR spectrum of (IV) there are absorption bands at 3350 cm^{-1} (hydroxy group), 1715-1730 cm^{-1} (C = O of an α-pyrone and C = O of an ester grouping), 1610, 1590, and 1510 cm^{-1} (aromatic nucleus), and 1410 and 1385 cm^{-1} (gem-dimethyl group).

The NMR spectrum of (IV) contains signals of the following structural elements:  $-\underset{\substack{|\\ O}}{C}\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$ (1.25, 1.30 ppm, singlets, 6H),  $-CH=C\begin{smallmatrix}CH_3\\ CH_3\end{smallmatrix}$ (1.66, 1.82 ppm, singlets, 6H, and 5.51 ppm, triplet, 1H), and $Ar-CH_2-CH-$ (3.59 ppm, multiplet, 2H, and 4.86 ppm, quartet, 1H). A signal with its center at 5.24 ppm is probably due to the proton of a phenolic hydroxy group. A three-proton singlet at 3.36 ppm (3H) is due to the presence in the molecule of (IV) of an aliphatic methoxy group. In the region of aromatic protons there are the same signals as in the spectrum of (III). On the basis of these facts (IV) can be considered as 3'-O-methylferudiol.

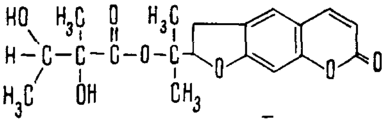


IV

Substance (V), $C_{19}H_{22}O_7$, mp 112°C, possesses the properties characteristic for dihydrofurocoumarins. In its IR spectra there are absorption bands at 3400 cm^{-1} (hydroxy group), 1725 cm^{-1} (C = O of an α-pyrone), 1625 and 1585 cm^{-1} (aromatic nucleus), and 1390 and 1350 cm^{-1} (gem-dimethyl group). The presence of a broad carbonyl band in the spectrum shows that the molecule of (V) also includes an ester grouping.

In the NMR spectrum of (V) in the region of aromatic protons there are two doublets with chemical shifts of 6.17 and 7.55 ppm, J = 10 Hz (1H each) due to protons in positions 3 and 4 of the coumarin nucleus. Singlets at 7.15 and 6.69 ppm (1H each) belong to the protons in positions 5 and 8, respectively. Accordingly, (V) is a 6,7-disubstituted coumarin.

In the region of aliphatic protons are observed the signals of a methylene group attached to an aromatic ring (3.29 ppm, doublet, 2H, J = 8 Hz) and of a methine proton in position 5', appearing in the weakest field (in the 5.27-5.65-ppm range, 1H) obviously because of the presence of an ester grouping adjacent to it. For the same reason, the protons of a gem-dimethyl group are found at 1.67, 1.73 ppm (6H). This spectrum also has a six-proton singlet at 1.24 ppm with secondary splitting (J = 1.5 Hz) due to the protons of two methyl groups adjacent to an oxygen atom. A complex multiplet in the range of 4.53-4.79 ppm (1H) is apparently due to a proton in an acid residue. A broadened singlet at 2.60 ppm (2H) can be assigned to the protons of two hydroxy groups probably present in the acid moiety of the molecule, which is confirmed by the results of the alkaline hydrolysis of (V) with 10% KOH. This forms a dihydrofurocoumarin (XIII) with mp 185-187°C shown to be identical by its IR and NMR spectra with marmesin, and an oily substance (XIV) identified by its NMR spectrum as 2,3-dihydroxyacrylic acid (singlet at 1.27 ppm, 6H; multiplet with its center at 4.51 ppm, 1H). Consequently, (V), which we have called lindiol, is an ester of marmesin and 2,3-dihydroxy-2-methylbutyric acid.



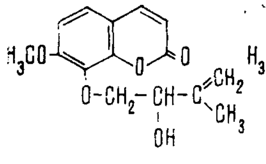
V

Substance (VI), $C_9H_6O_3$, mp 231-233°C, was identified by its IR and NMR spectra as umbelliferone.

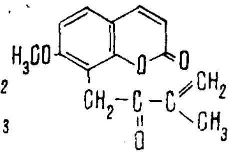
Substances (VII), $C_{15}H_{16}O_5$, mp 98.5-101°C, and (VIII), $C_{15}H_{14}O_4$, mp 92-94°C, which have been called ferudenol and prangone, respectively, possess a blue fluorescence and belong to the group of 7,8-disubstituted coumarins.

The IR spectrum of (VII) has absorption bands at 3500 cm^{-1} (hydroxy group), 1725 cm^{-1} (C = O of an α-pyrone), and 1620, 1570, and 1500 cm^{-1} (aromatic nucleus). The presence of a hydroxy group was confirmed by the formation of an acetyl derivative (XV), $C_{17}H_{18}O_6$, the IR spectrum of which lacked the absorption band of an OH group.

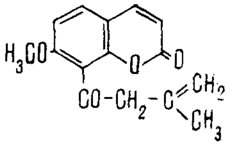
The NMR spectrum of (VII) showed the signals of the protons of a methyl group on a double bond (1.78 ppm, singlet, 3H), a hydroxy group (1.87 ppm, singlet, 1H), an $Ar-O-CH_2-CH-$ grouping (4.40 ppm, J = 6.5 Hz, doublet, 2H, and 2.87 ppm, triplet, 1H), and a methoxy group in position 7 (3.91 ppm, singlet, 3H). One-proton singlets at 4.76 and 4.87 ppm are apparently due to the presence of a methylene group of a double bond in the molecule of (VII). In the region of aromatic protons four doublets are observed at 6.22, 7.60 ppm (J = 9.5 Hz) and 7.30, 6.84 ppm (J = 9 Hz), corresponding to protons at C_3, C_4, C_5, and C_6 of the coumarin nucleus. The facts given enable us to propose for (VII) the most probable structure of 8-(2'-hydroxy-3-methylbut-3-enyloxy)-7-methoxycoumarin.



VII



VIII



XVIII

The NMR spectrum of (VIII) contains the signals of the protons of a $-C\begin{matrix}CH_2\\CH_3\end{matrix}$ grouping (1.72 ppm, singlet, 3H; 5.20 and 5.28 ppm, singlet, 1H each) and a $-OCH_3$ group in position 7 (3.95 ppm, singlet, 3H). The signals of the protons of a methylene group attached to an aromatic ring appear at 3.54 ppm (doublet, 2H, J = 7 Hz). In the region of aromatic protons the same signals are observed as in the spectrum of (VII), which shows that prangone is also a 7,8-disubstituted coumarin and has the structure (VIII). This is confirmed by the production of isomeransin (XVI), $C_{15}H_{16}O_4$, mp 64–66°C, when (VIII) was treated with 20% sulfuric acid.

It must be noted that structure (VIII) has recently been proposed for the coumarin murrayone (XVII) isolated from Murraya exotica Linn [2]. However, on comparing the results we have obtained and those given by Lakshmi et al. [2] we came to the conclusion that these substances are not identical, since the melting points and the NMR spectra (in deuteroacetone and in $CDCl_3$) of (VIII) and in (XVII) differ sharply. In its composition and melting point, substance (XVII) corresponds to the known coumarin micropubescin (XVIII) isolated from the bark of Micromelum pubescens Linn [3, 4], but the authors concerned, on the basis of differences in the IR spectra of (XVII) and (XVIII) and the depression of the melting point of a mixture did not identify (XVII) with micropubescin (XVIII). It is possible that (XVII) and (XVIII) are optical antipodes, for which the IR spectra do in fact differ, and which some times give a depression of the melting point.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer (mulls in paraffin oil), the NMR spectra on a Varian HA-100D spectrometer ($CDCl_3$ and deuteroacetone, 0 – HMDS), and the mass spectra on an LKB-9000 instrument. The melting points were determined on a Koffler block. The elementary analyses of all the compounds corresponded to the calculated figures.

For the isolation of (II-IV) see [1].

Isolation of (V) and (VI). These compounds, like (III) and (IV), were obtained from fractions 22-26. As compared with the other components of the plant studied, substances (III-VI) are distinguished by their very small amount (about 0.02% relative to the resin) as they form a mixture difficult to separate. Consequently, to isolate them in the individual state we used preparative thin-layer chromatography (Al_2O_3, activity grade V, ethyl acetate system; size of the plates 30 × 40 cm). In this way we obtained (V) with mp 112°C (from benzene) and (VI) with mp 231-233°C (from chloroform).

Isolation of (VII) and (VIII). A crystalline mixture of (VII) and (VIII) (0.65 g) obtained in the primary chromatography of the resin from the roots of Prangos ferulacea growing in Armenia [5] was chromatographed on a microcolumn of alumina (30 g, activity grade III). Elution was performed with benzene (fractions 1-5), a mixture of benzene and chloroform (fractions 6-10), and chloroform (fractions 10-14). The benzene fractions, after the solvent had been distilled off, yielded (VIII) with mp 92-94°C (from petroleum ether), and the chloroform fractions yielded (VII) with mp 98.5-101°C (from benzene).

Acid Cleavage of (II). A solution of 0.1 g of (II) in 15 ml of glacial acetic acid was treated with five drops of concentrated sulfuric acid and heated on the water bath for 1.5 h. Then it was worked up by the usual method. This gave substance (IX) with mp 250-251°C (from ether), identical with xanthotoxol.

Alkaline Hydrolysis of (III). A mixture of 0.72 g of the (III) and 30 ml of 10% KOH in methanol was heated for 30 min, and then the methanol was evaporated off and the residue was dissolved in water. After acidification with concentrated HCl, the reaction product was extracted with ether. The ethereal extract was washed twice with water and dried over sodium sulfate. The solvent was distilled off under vacuum. An oily substance (XI) was isolated. The mother solution after the isolation of (XI) was distilled under vacuum, and the distillate was saturated with NaCl and extracted with ether. Distillation of the solvent yielded (X) with mp 67-69°C, identical with that of senecioic acid.

Methylation of (XI). The substance obtained (0.42 g) was methylated by the usual method with dimethyl sulfate in acetone with the addition of potassium carbonate for 12 h. Compound (XII) with mp 126-127°C (from benzene), identical with meransin hydrate, was isolated.

Alkaline Hydrolysis of (V). The hydrolysis of 0.45 g of (V) was performed as described above for (III). This gave marmesin (XIII) with mp 185-187°C (from benzene) and an oily substance (XIV), identified by its NMR spectrum as 2,3-dihydroxy-2-methylbutyric acid.

Acetylation of (VII). Compound (VII) (0.1 g) was acetylated with acetic anhydride (3 ml) in pyridine (1 ml) for 2 h. After the usual working up of the reaction mixture, a monoacetate (XV) was obtained in the IR spectrum of which there was no absorption band of a hydroxy group.

Isomerization of (VIII). A mixture of 0.2 g of (VIII) and 30 ml of 20% sulfuric acid was heated for 1 h. After the usual working up, (XVI) was isolated with mp 64-66°C (from petroleum ether); it was identical with isomeransin.

SUMMARY

From a methanolic extract of the roots of *Prangos ferulacea* (L) Lindl., growing in the Nakhichevan ASSR, in addition to the compounds found previously, another six substances (I-VI) have been isolated, of which (I) and (VI) have been identified as, respectively, meransin hydrate monoacetate, found for the first time in nature, and umbelliferone: and in the study of a crystalline mixture obtained from the resin of the roots of the plant under investigation collected in Armenia, two coumarins – (VII) and (VIII) – have been isolated.

On the basis of a study of IR, NMR, and mass spectra and chemical properties, the structures of the six new coumarin derivatives (II-V, VII, and VIII) have been established. Compound (II) has the structure of 8-(3''-methylbutenyloxy)furo-2',3': 7,6-coumarin and has been called feruliden; (III) is 7-hydroxy-8-(3'-hydroxy-2'-senecioyloxyisopentyl)coumarin and has been called ferudiol; (IV) is 7-hydroxy-8-(3'-methoxy-2'-senecioyloxyisopentyl)coumarin; (V) is 5'-[1''-(2''',3'''-dihydroxy-3'''-methylbutyroyloxy)-1''-methylethyl]-4',5'-dihydrofuro-2',3': 7,6-coumarin and has been called lindiol; (VII) is 8-(2'-hydroxy-3'-methylbut-3'-enyloxy)-7-methoxycoumarin and has been called ferudenol; (VIII) is 7-methoxy-8-(3'-methyl-2'-oxobut-3'-enyl)coumarin and has been called prangone.

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