PRANFERIN – A NEW COUMARIN FROM THE ROOTS OF Prangos ferulacea

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Continuing a chemical study of the coumarin compounds from the roots of Prangos ferulacea (L.) Lindl., we have isolated an optically inactive substance $C_{18}H_{22}O_5$ with mp 167.5–169°C and mol. wt. 318 (mass spectrometrically), which we have called pranferin.

In UV light, pranferin (I) possesses a bright blue fluorescence and it gives a UV spectrum with absorption maxima at 246, 256, and 320 nm (log ε 3.52, 3.56, 4.18). This shows that it is in fact a coumarin.

The IR spectrum of I (Fig. 1) has a broad band at 1710–1730 cm^{-1} (C = O of an α-pyrone ring) and also bands at 1505, 1570, and 1610 cm^{-1} (aromatic nucleus), and its UV and IR spectra are very similar to those of osthole and meranzin hydrate, which permits (I) to be assigned to the 7,8-disubstitued coumarins.

When (I) was oxidized with chromium trioxide in glacial acetic acid, a substance (II) with mp 253°C was obtained which was identified by its IR spectra and the absence of a depression in admixture with the ostholic acid obtained previously from osthole and meranzin hydrate [1]. This shows that I is a 7-methoxycoumarin in position 8 of which there is a substituent attached to the ring through a $-CH_2-$ group.

The reduction of I with sodium borohydride in methanol gave a substance III with mp 100–102°C. Its IR spectrum had absorption bands at 3490 cm^{-1} (OH group), 1715 cm^{-1} (α-pyrone ring), and 1500, 1570, and 1615 cm^{-1} (aromatic nucleus). Consequently, in the side chain of I there is an aliphatic C = O group which can be reduced to a hydroxy group.

When compound I was treated with a mixture of glacial acetic and concentrated sulfuric acids, compound IV with mp 115–117°C was obtained. Its IR spectrum contained bands at 3420 cm^{-1} (hydroxy group), 1725 cm^{-1} (α-pyrone ring), and 1500, 1570, and 1610 cm^{-1} (aromatic ring). The acetylation of IV with acetic anhydride in pyridine led to a monoacetyl derivative V with mp 218–220°C, the IR spectrum of which lacked the absorption band of a hydroxy group. The ease of acetylation shows that the OH group is either primary or secondary. The occurrence of acid cleavage shows the presence of an ether group in I.

In the NMR spectrum of I (Fig. 2), in the weak field there are four doublets with chemical shifts δ 6.20 and 7.60 (J = 9 Hz) and 7.33 and 6.84 (J = 8.3 Hz) belonging to the protons of the coumarin nucleus in positions 3 and 4 and positions 5 and 6, respectively [2, 3]. These results confirm the structure of compound I as a 7,8-disubstituted coumarin. A quartet in the 4.06 ppm region (with an intensity of one proton unit) and two quartets at 3.05 ppm (with an intensity of two proton units) can be assigned to the CH and CH_2 groups in the $\text{—O—}\underset{|}{\text{CH}}\text{—CH}_2\text{—Ar}$ fragment. The structure of the signals is determined by the two vicinal constants (J_1 = 4.7 Hz and J_2 = 7.6 Hz) and the geminal constant for the $-CH_2-$ group, J_{gem} = 13.5 Hz. A signal at 3.92 ppm corresponds to a methoxy group in position 7. In the 1.19–1.29 ppm region there are three singlet signals (of three proton units each) which must be assigned to the methyl groups in a $(CH_3)_3C-O-$ grouping, since the elementary composition does not permit any other combination with three methyl groups attached to quaternary carbon atoms. For the singlet at 1.43 ppm (with an intensity of three proton units) only an assignment to a CH_3CO group of the side chain is possible, although the value of δ obtained is lower than that generally observed for such groups. It may be assumed that this displacement of the signal

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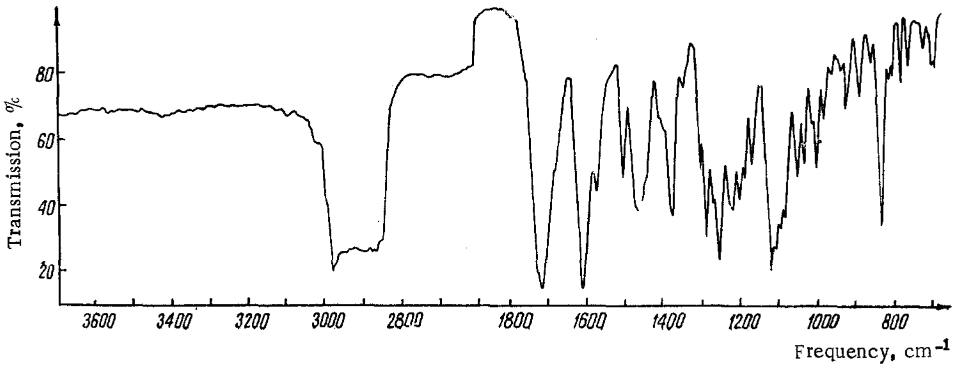


Fig. 1. IR spectrum of pranferin.

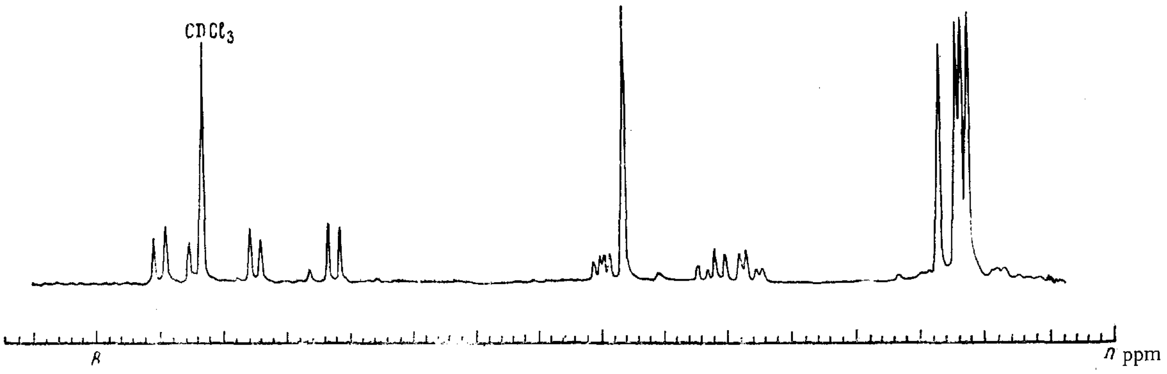
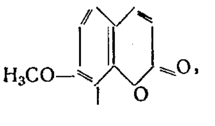
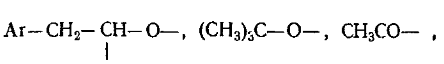


Fig. 2. NMR spectrum of pranferin.

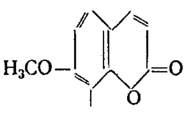
in the upfield direction is due to the presence of the CH_3CO group above the ring in the region of screening by the aromatic ring.

Thus, the combination of chemical and spectral information shows the presence of the following groupings in the molecule of compound I:

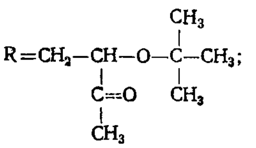



$Ar-CH_2-\underset{|}{C}H-O-$, $(CH_3)_3C-O-$, CH_3CO- ,

from which the structure of compound I and derivatives II-V follow clearly:

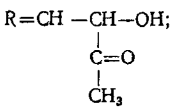


I



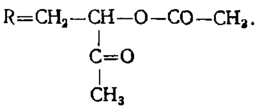
$R=CH_2-CH(COCH_3)-O-C(CH_3)_3$;

IV



$R=CH-CH(OH)-COCH_3$;

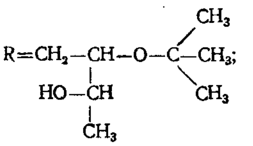
V



$R=CH_2-CH(COCH_3)-O-CO-CH_3$.

II $R=CH_2-COOH$;

III



$R=CH_2-CH(CH(OH)CH_3)-O-C(CH_3)_3$;

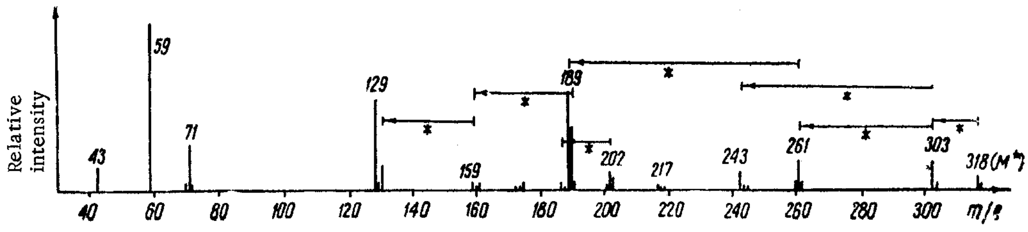
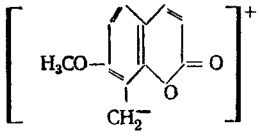


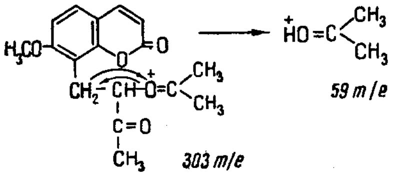
Fig. 3. Mass spectrum of pranferin.

The structure proposed agrees well with the mass spectra.

In the mass spectrum of compound I (Fig. 3) the molecular ion with m/e 318 and fragments corresponding to the decomposition of an ether – by the cleavage of an α-C–O–C bond (peaks at 303, 129, and 189 m/e) – are clearly shown. The further decomposition of the ion with m/e 189 is analogous to the decomposition of the fragment with the structure



m/e 189, found in the spectra of compounds IV, meranzin hydrate, and ulopterole [4]. In the spectrum of I there is a strong peak with m/e 59 which may be due to the cleavage of an α-bond with the migration of hydrogen that is characteristic for an ether [5] in the 303 m/e fragment (M^+-CH_3).



The presence in the spectrum of peaks at 303 and 59 m/e is in harmony with the existence of an $O-C(CH_3)_3$ group in the molecule.

Mass spectra also confirm the structure of IV, giving a molecular weight of 262 m/e and also showing peaks of the fragments M–17 (M^+-OH) and M–18 (M^+-H_2O), which are characteristic for hydroxyl-containing compounds.

EXPERIMENTAL

Isolation of Pranferin (I). Five grams of the mixture of crystalline substances obtained from the 22nd and 23rd fractions after the isolation of pranferol [6] was chromatographed on KSK silica gel (30 g). Elution was performed with benzene, benzene–chloroform, and chloroform. The volume of each fraction was 50 ml. The solvent was distilled off from the benzene fractions to give I with mp 167.5-169°C (from benzene), $[\alpha]_D^{16}$ ± 0° (c 3.88; chloroform), R_f 0.70 [Al_2O_3, activity grade II, ethyl acetate–benzene (1 : 4)].

Found, %: C 67.46; 67.51; H 6.79; 6.86. Mol. wt. 318 (mass spectrometrically). Calculated for $C_{18}H_{22}O_5$. %: C 67.92; H 6.91. Mol. wt. 318.

Oxidation of I. A solution of 0.12 g of I in 5 ml of glacial acetic acid was treated with 0.2 g of chromic anhydride in 10 ml of 50% acetic acid and the mixture was left at room temperature for 48 h. From the reaction products a substance II, $C_{12}H_{10}O_5$, mp 253°C (from ethanol) was isolated. A mixture of II with an authentic sample of ostholic acid obtained similarly from natural osthole and meranzin hydrate gave no depression of the melting point.

Reduction of I. A solution of 0.031 g of I in 10 ml of methanol was treated with 0.2 g of sodium borohydride, and the mixture was left for 3 days. Then it was acidified with 20% sulfuric acid, and the reaction product was extracted with ether. The ethereal solution was washed with water and dried with anhydrous sodium sulfate. The resinous residue after the distillation of ether was separated preparatively in thin layers of alumina. This gave substance III, $C_{18}H_{24}O_5$, mp 100-102°C (from petroleum ether), R_f 0.24 [Al_2O_3, activity grade II, ethyl acetate–benzene (1 : 4)].

Acid Cleavage of I. A solution of 0.0742 g of I in 10 ml of glacial acetic acid was treated with ten drops of Conc. sulfuric acid and the mixture was heated in the water bath for 45 min. Then it was diluted with water and extracted with ether. The ethereal solution was washed twice with water and was dried with anhydrous sodium sulfate. The solvent was distilled off and the residue was deposited on a microlayer of alumina. Elution was carried out with petroleum ether and petroleum ether–chloroform. Elution with the mixed solvent gave IV, $C_{14}H_{14}O_5$, mp 115-117°C (from a mixture of chloroform and petroleum ether), R_f 0.25 [Al_2O_3 of activity grade II, ethyl acetate–benzene (1 : 2)].

Acetylation of IV. A mixture of 0.0059 g of IV, 2 ml of acetic anhydride, and 0.5 ml of pyridine was heated for 4 h. Then it was cooled, diluted with water, and extracted with ether. The ethereal extracts were washed with water and dried with anhydrous sodium sulfate. The ether was distilled off and the residue was recrystallized from benzene. This gave substance V, $C_{16}H_{16}O_6$, mp 218-220°C (from petroleum ether), R_f 0.63 [Al_2O_3 of activity grade II, ethyl acetate–benzene (1 : 4)]. IR spectrum, cm^{-1}: 1750, 1740, 1615, 1570, 1505, 1380, 1280, 1250, 1120, 1080, 1040, 830.

The IR spectra were taken on a UR-10 spectrometer (as mulls in paraffin oil), the UV spectrum on an SF-4A spectrophotometer (as a solution in ethanol), the NMR spectrum on a JNM-4H-100 spectrometer, and the mass spectra on an MKh-1303 instrument at an ionizing voltage of 30 eV. The melting points were determined on a Kofler block.

SUMMARY

From the roots of *Prangos ferulacea* (L) Lindl. a new coumarin has been isolated, $C_{18}H_{22}O_5$, mp 167.5-169°C (from benzene) $[\alpha]_D^{16} \pm 0°$ (c 3.88; chloroform), and it has been called pranferin.

By a study of its UV, IR, NMR, and mass spectra and chemical properties, its structure has been established as 8-(2'-acetyl-2'-tert-butoxyethyl)-7-methoxycoumarin.

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