THE STRUCTURES OF DRUPACIN AND DRUPANIN – NEW COMPONENTS OF Psoralea drupaceae

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Psoralea drupaceae Bge.(drupe scurfpea) affects the sex function of animals [1]. Consequently, the study of the chemical composition of this plant is of great interest.

In 1960, V. G. Shimanov isolated from the fruit of the scurfpea an active crystalline substance which he called drupacin[2] and for which the composition $C_{11}H_{24}O_7$ was put forward, without, however, the results of elementary analysis being given. This substance was apparently not a pure compound: its physical constants were not determined and its chemical nature and structure were not established.

Using Shimanov's method [2], we have isolated a substance corresponding to the description of drupacin and have purified it and subjected it to chemical study. Drupacin (I) is a crystalline substance with the composition $C_{14}H_{16}O_3$, sparingly soluble in ethanol, acetone, chloroform, and carbon tetrachloride. It has an acid nature: on treatment with sodium carbonate it passes into solution, and on acidification it is precipitated unchanged; with lead acetate it forms a water-insoluble salt, and on methylation it forms a monomethyl ester $C_{15}H_{18}O_3$. On titration with caustic soda it reacts with 1 mole of the latter, while it gives no reaction with ferric chloride and diazotized sulfanilamide. These properties show that drupacin is an organic acid. Of the three oxygen atoms, two are present in a carboxy group and the third is most probably present in an ether grouping.

The UV spectrum of drupacin shows maxima with λ_{max} 316, 234, and 217 nm ($\log \varepsilon$ 4.17, 3.95, and 3.99). In the presence of alkali, the longwave band undergoes a hypsochromic shift by 26 nm with a simultaneous increase in intensity, which shows the absence of a phenolic hydroxyl from the substance and the presence of a carboxy group. The presence of the latter was confirmed by the formation of a monomethyl ester.

The IR spectrum of (I) (Fig. 1a) shows absorption bands at 1580 and 1625 cm^{-1} and also at 875 and 832 cm^{-1} (1,3,4-substituted aromatic ring), 1680 cm^{-1} (carbonyl of an α,β-unsaturated acid conjugated with an aromatic nucleus), and 890 cm^{-1} (gem-dimethyl group in a six-membered ring). In the IR spectrum of the methyl ester of drupacin, the band at 1680 cm^{-1} has disappeared and a band has appeared at 1715 cm^{-1}, which corresponds to the carbonyl group of the ester of an unsaturated acid.

In the NMR spectrum of the methyl ester of (I) (Fig. 2) doublets are found in the weak field at 7.52 and 6.17 ppm, each of 1 H (J = 16 Hz), due to olefinic protons conjugated with an Ar–CH=CH–COO grouping. The high value of the spin–spin coupling constant shows that they are present in the trans position. Doublets at 7.17 and 6.67 ppm (1H, J = 8 Hz) are caused by aromatic ortho-interacting protons. In addition, a singlet is found at 7.14 ppm (1H), superposed on one of the components of the first doublet, which is due to an isolated aromatic proton. Two two-proton triplets at 2.67 and 1.7 ppm (J = 7 Hz) and a singlet at 1.28 ppm (6H) are due, respectively, to the protons of two neighboring methylene and gem-dimethyl groups on a quaternary carbon atom present in the Ar–CH_2–CH_2–$C(CH_3)_2$–O grouping. A singlet at 3.70 ppm with an intensity of 3 H is due to the protons of the methyl group of the ester of (I).

The facts given permit the conclusion that drupacin is based on cinnamic acid disubstituted in the aromatic nucleus to which an isoprenoid nucleus in the form of a dimethylpyran ring is attached. The position of the substituent follows from the IR spectrum of (I). The longwave maximum of drupacin is at 316

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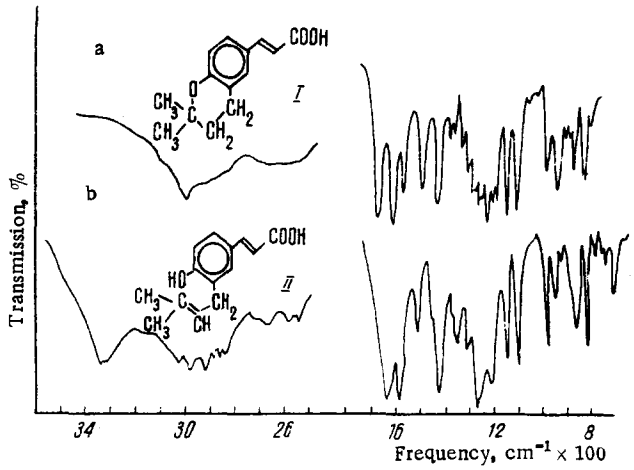

Fig. 1. IR spectrum of drupacin (a) and drupanin (b) (KBr).

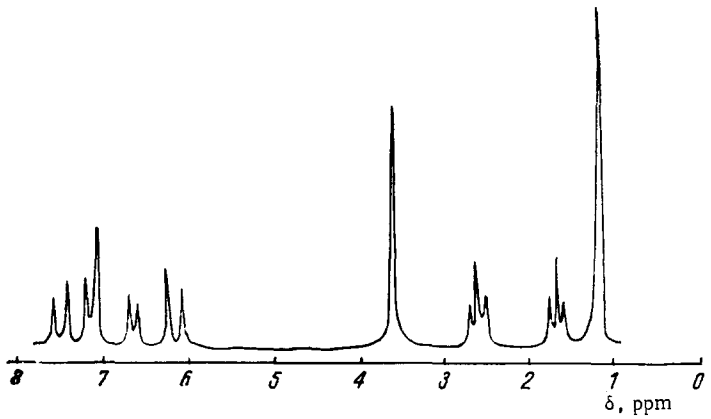

Fig. 2. NMR spectrum of the methyl ester of drupacin ($CDCl_3$).

nm, which corresponds to the calculated value for cinnamic acid substituted by oxygen in the para position and containing a meta-alkyl substituent (calculated λ_{max} 314 nm). Consequently, drupacin has the structure (I).

In addition to drupacin, from the acid fraction of the seeds of the scurfpea by chromatography on silica gel we isolated a second substance, with the composition $C_{14}H_{16}O_3$, which we have called drupanin (II). Its chemical properties are also those of an acid, but, in contrast to (I), it gives a reaction with ferric chloride, i.e., it contains a phenolic hydroxyl.

The UV spectrum of (II) shows the same absorption bands as that of drupacin with somewhat different intensities – λ_{max} 318, 235, and 216 nm ($\log \varepsilon$ 4.87, 4.72, and 4.75). The similarity of the UV spectra of (I) and (II) shows that these substances have the same chromophore.

In the IR spectrum of (II) (Fig. 1b) there are bands at 1520 and 1595 cm^{-1} and also at 822 and 865 cm^{-1} (1,3,4-substituted benzene ring), 1665 cm^{-1} (carbonyl of an α,β-unsubstituted acid), and 790 cm^{-1} (β-isopropylidene group).

The methylation of drupanin with diazomethane for 2 min gave a monomethyl ether $C_{15}H_{18}O_3$. This did not give a reaction with ferric chloride and was soluble in sodium carbonate solution. Its IR spectrum retained the carbonyl band of an acid, and there was no bathochromic shift of the longwave maximum in the UV spectrum in the presence of alkali. This shows that under the conditions mentioned methylation took place only at the phenolic hydroxyl. More prolonged methylation yielded a mixture of products.

In its NMR spectrum, the chemical shifts of the signals in the weak-field region are similar to those for the methyl ester of (I): doublets at 7.57 and 6.20 ppm (J = 16 Hz) (the α- and β-olefinic protons of cinnamic acid), quadruplet at 6.77 and 7.16 ppm (J = 9 Hz) and singlet at 7.20 ppm (aromatic protons). Consequently, drupanin is also a derivative of a 3-alkyl-4-hydroxycinnamic acid and differs from drupacin

by the structure of the substituents. One of them is a free phenolic hydroxyl, and the second is a C_5H_9 residue.

In the spectrum given above, in addition to the signals of the aromatic protons there are a triplet at 5.25 ppm (1H, J = 6.6 Hz), a doublet at 3.26 ppm (2H, J = 6.6 Hz), and a singlet at 1.67 ppm (6H), corresponding to the protons in an $Ar-CH_2-CH=C(CH_3)_2$ grouping, from which it follows that drupanin has the structure (II).

On being heated with concentrated HBr, drupanin underwent cyclization into drupacin, while heating with 5% aqueous HCl caused no cyclization. These results, on the one hand, confirm the proposed structure and, on the other hand, show that the formation of drupacin does not take place during isolation, i.e., it is a natural substance.

EXPERIMENTAL

The UV spectra were taken on a Hitachi spectrophotometer (in ethanol), the IR spectra on a UR-20 instrument (tablets with KBr), the mass spectra on an MKh-1303 mass spectrometer, and the NMR spectra on a JNM-4H-100/100 MHz instrument (in deuterochloroform), the chemical shifts being given in the δ scale from the signal of HMDS taken as 0.

The purity of the substances and the courses of the reactions were checked by thin-layer chromatography in a fixed layer of silica gel with the n-hexane–benzene–methanol (5 : 4 : 1) system, the spots being revealed with iodine vapor and with a 1% solution of vanillin in concentrated sulfuric acid. The results of elementary analysis corresponded to the calculated figures.

Isolation of Drupacin. The dried and comminuted fruit (1.5 kg) was steeped with 1.5-liter portions of ether three times. The ethereal extract was washed with 5% caustic soda solution. The extract was acidified with 5% hydrochloric acid solution and heated to the boil. The solution was cooled and treated with ether. Concentration of the ethereal extract yielded acicular crystals with mp 205-206°C (from methanol), M^+ 232, R_f 0.5 (yield 0.5 g; 0.03% of the raw material).

Isolation of Drupanin. The dried and comminuted fruit (2 kg) was steeped with ether. The ethereal extract was treated three times with 5% sodium bicarbonate solution. These extracts were combined and acidified with 2% HCl, and the acids were extracted with ether. After the elimination of the solvent, 4 g of a solid mass was obtained which was chromatographed on a column of KSK silica gel (25 cm high and 2.5 cm in diameter), the substances being eluted with benzene–ether (9 : 1). Distillation of the solvent yielded 0.7 g (0.035%) of acicular crystals with mp 147-148°C, M^+ 232, R_f 0.25.

Methylation of Drupacin. A solution of 0.10 g of the substance in 15 ml of methanol was acidified with 5 ml of conc. sulfuric acid and heated in the water bath for 4 h. After the end of the reaction, the solvent was distilled off, and the residue was dissolved in ether and washed with water. The ether was driven off, and a crystalline substance was isolated with mp 69-70°C (from methanol), M^+ 246, R_f 0.8 (yield 0.08 g).

Methylation of Drupanin. To a solution of 0.12 g of the substance in 5 ml of ether was added 10 ml of an ethereal solution of diazomethane in small portions over 2 min. The solvent was evaporated off at room temperature in vacuum. The residue consisted of a crystalline product with mp 85-86°C (petroleum ether–diethyl ether), M^+ 246, R_f 0.55.

Cyclization of Drupanin. A small crystal of the substance was dissolved in 1 ml of glacial acetic acid, 0.5 ml of conc. HBr was added, and the liquid was heated for 2 h. Then it was diluted with water and the reaction product was extracted with ether and washed with water. The residue after the distillation of the solvent consisted of a single substance with R_f 0.5 corresponding to drupacin.

SUMMARY

The physicochemical properties and results of spectroscopy have enabled the empirical formula of drupacin, isolated previously from the seeds of Psoralea drupaceae, to be corrected and its structure to be established. It is 2',2'-dimethyl-3',4'-dihydropyrano(5',6':3,4)-trans-cinnamic acid.

In addition to drupacin, a new component with the composition $C_{14}H_{13}O_3$, mp 147-148°C has been isolated; this has been named drupanin and has the structure of 4-hydroxy-3-(3'-methylbut-2'-enyl)-trans-cinnamic acid.

LITERATURE CITED

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