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STRUCTURE AND CONFIGURATION OF CAUFERININ

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Continuing a study of the coumarins of the roots of *Ferula conocaula* Korov. [1, 2], from the total extractive substances we have extracted a new terpenoid coumarin with the composition $C_{22}H_{32}O_6$, M^+ 416, mp 204-206°C, $[\alpha]_D^{20}$ +37.5° (c 0.5; ethanol), which we have called cauferinin. It is readily soluble in acetone, ethanol, and pyridine, sparingly soluble in chloroform and water, and insoluble in ether.

The UV spectrum has maxima at λ_{max} 218, 244, 255, and 328 nm (log ε 4.22, 3.80, 3.85, and 4.08) which are characteristic for a 7-hydroxy-substituted coumarin chromophore, and the IR spectrum has absorption bands of an OH group (3400 cm^{-1}), of the carbonyl of an α-pyrone (1713 cm^{-1}), and of an aromatic nucleus (1618, 1515 cm^{-1}).

Treatment of cauferinin with acetic anhydride in pyridine yielded cauferinin diacetate with the composition $C_{28}H_{36}O_8$, M^+ 500, the IR spectrum of which retained the absorption band of an OH group. These facts show that the terpenoid part of cauferinin contains three hydroxy groups, one of which is tertiary while the other two are secondary. The presence of hydroxy groups was also confirmed by the mass spectrum of cauferinin [m/e 416 (M^+), 398 ($M - H_2O$)$^+$, 380 ($M - 2H_2O$)$^+$, 255 ($M - RO$)$^+$, 237 ($M - RO - H_2O$)$^+$, 219 ($M - RO - 2H_2O$)$^+$, 201 ($M - RO - 3H_2O$)$^+$, 161 (RO)$^+$, 162 (ROH)$^+$], in which there are fragments corresponding to the successive elimination of three molecules of water.

The PMR spectrum (C_5D_5N) of cauferinin has the signals of methyl groups on quaternary carbon atoms — singlets at 1.04 (3H), 1.37 (6 H), and 1.85 ppm (3 H) — and a multiplet at 3.57 ppm (2 H) due to hemihydroxylic protons. A multiplet in the 4.25 ppm region (2 H) represents the methylene protons on a —CH_2—O—R grouping. In addition, in the weak-field region there are one-proton doublets at 6.20 and 7.57 ppm (J = 10 Hz), 7.16 ppm (J = 2.5 Hz), and 7.32 ppm (J = 8.5 Hz) due to the H_3, H_4, H_8, and H_5 protons, respectively; a quartet at 6.92 ppm (1 H, J_{ortho} = 8.5 Hz, J_{meta} = 2.5 Hz) is due to the H_6 proton of the coumarin ring.

It must be mentioned that the PMR spectrum of cauferinin diacetate has signals with similar chemical shifts and multiplicities to those of cauferin diacetate [2] and differs only by the fact that in place of the signals of the protons of an exocyclic methylene at 4.56 and 4.89 ppm (in cauferin diacetate) there is a singlet at 1.28 ppm caused by the presence of a hemihydroxylic methyl group. From the facts given above, it may be concluded that cauferinin is cauferin hydrated at C_2' [2]. This is in harmony with the mass spectrum of cauferinin which includes a peak with m/e 398 corresponding to the fragment after the ejection of one molecule of water.

The dehydration of cauferinin with sulfuric acid in ethanol yielded an anhydro derivative with the composition $C_{24}H_{30}O_5$, M^+ 398. A comparison of the physicochemical constants and spectral characteristics (IR, PMR) of the latter and of cauferin showed that they were completely identical. Consequently, in the cauferinin molecule there are, as in cauferin, hydroxy groups at C_4' and C_6' and they are oriented equatorially. The substituent —CH_2—OR at C_1' also has the equatorial orientation.

The formation of cauferin in the dehydration of cauferinin also showed the equatorial orientation of the hydroxy group and the axial orientation of the methyl group at C_2', since it is just in this case that the formation of an exocyclic double bond is observed [3, 4].

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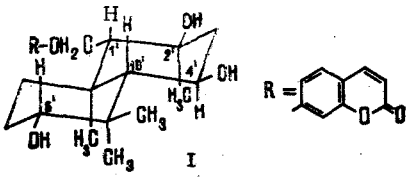
Summing the facts given above, and also taking biogenetic considerations into account, for cauferinin we propose the structure and relative configuration (I) with the trans-non-steroid linkage of the rings of the decalin nucleus. Consequently, the coumarins—cauferin [2], ferocaulin, ferocaulinin, ferocaulidin, and ferocaulicin [1]—have similar configurations.



I

It must be mentioned that all the coumarins isolated from *Ferula conocaula* [5-8] are interconnected biogenetically in sequence. They are ethers of umbelliferone with bicyclic sesquiterpene alcohols — diols, triols, and tetraols.

EXPERIMENTAL

The conditions for recording the spectra have been described previously [1]. For chromatography we used type KSK silica gel. The individualities of the substances and the course of the reactions were checked by the TLC method on Silufol plates in the chloroform—ethanol (4:1) system.

Isolation of Cauferinin. A solution of 500 g of the viscous ethanolic extract of the roots of *F. conocaula* in 300 ml of ethanol was diluted twofold with water and extracted with ether. Then the aqueous ethanolic part was extracted with n-butanol and the butanol was distilled off. This gave 40 g of extractive substances. Of this, 30 g was mixed with 30 g of silica gel, placed on a column of silica gel (6 × 110 cm) and eluted with chloroform—ethanol (10:1), 400-ml fractions being collected. When the eluate was concentrated, fractions 19-26 yielded 0.19 g of a crystalline substance $C_{24}H_{32}O_6$, M^+ 416, mp 204-206°C, $[\alpha]_D^{20}$ +37.5° (c 0.5; ethanol).

Acetylation of Cauferinin. The substance (50 mg) was kept in 2 ml of a mixture of acetic anhydride and pyridine (1:1) at 20°C for 72 h. After the usual working up, 38 mg of a substance $C_{28}H_{36}O_8$ was obtained with M^+ 500.

PMR spectrum: 0.90 s, 3 H; 0.99 s, 3 H; 1.04 s, 3 H [$C_{5',9'}$—$(CH_3)_3$]; 1.28 s, 3H ($C_{2'}$—CH_3); 2.01 s, 6 H [$C_{4',6'}$—$(OCOCH_3)_2$]; 4.15 m, 2 H ($C_{1'}$—CH_2); 4.43 m, 1 H ($C_{6'}$—H); 5.13 s, 1 H ($C_{4'}$—H); 6.18 d, 1 H, $J_{3,4}$ = 9.5 Hz (H_3); 6.78 q, 1 H, $J_{6,5}$ = 8.5 Hz, $J_{6,8}$ = 2.5 Hz (H_6); 6.82 d, 1 H, $J_{8,6}$ = 2.5 Hz (H_8); 7.30 d, 1 H, $J_{5,6}$ = 8.5 Hz (H_5); 7.59 d, 1 H, $J_{4,3}$ = 9.5 Hz (H_4).

Dehydration of Cauferinin. A solution of 68 mg of the substance in 3 ml of 10% sulfuric acid in methanol was heated in the water bath for 1 h. Then it was eluted with water and extracted with ether and the product was chromatographed on silica gel. Elution with hexane—chloroform (1:1) gave 28 mg of a substance $C_{24}H_{30}O_5$, M^+ 398, with mp 104-106°C.

SUMMARY

From the roots of *Ferula conocaula* Korov. a terpenoid coumarin of the iresane series with three hydroxy groups has been isolated which has been called cauferinin.

On the basis of the result of a study of its chemical and spectral characteristics and its conversion into cauferin, the structure and relative configuration (I) has been put forward for cauferinin.

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ACETYLORIENTIN — A C-GLYCOSYLFLAVONE FROM *Hypericum hirsutum*

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From the epigeal part of *Hypericum hirsutum* L. (hairy St. John's wort) we have isolated a number of flavonoid compounds, two of which have proven to be C-glycosylflavones [1]. There are no reports on the presence of flavones in species of the genus *Hypericum* L., with the exception of one on the chromatographic detection of luteolin in *H. hirsutum* [2]. Consequently, the compounds orientin and homoorientin that we have isolated are the first representatives of this type of flavonoid found in the genus *Hypericum*.

Continuing a study of the flavonoid complex of the herb hairy St. John's wort, we have isolated a flavonoid glycoside acylated with acetic acid (I).

From the results of qualitative reactions, fluorescence in UV light, and the Bryant test, it was assigned to the flavone glycosides [3, 4]. The intensity of the absorption $[E^{1\%}_{1cm}]$ = 393 characterized (I) as a monoside [5]. Analysis of the UV spectra showed four free hydroxy groups, in positions 3', 4', 5 and 7 [5, 6]. Acid treatment gave an intermediate product (II), which isomerized with the formation of a new substance having higher R_f values. No sugar and aglycone were detected as a result of this process. Alkaline hydrolysis gave only substance (II). These results show that the compound isolated is an acylated 8-C-glycosylflavone. The position of attachment of the carbohydrate moiety at C_8 was established on the basis of the chromatographic behavior of the isomers on acid hydrolysis and the presence of signals at 6.62, 1.75, and 1.95 ppm in the PMR spectrum of the full acetate of (I) (Fig. 1 and Table 1) which must be assigned to the H-6 protons and the 2"- and 6"-OAc groups, respectively (in acetate of 6-C-glycoflavonoids the signals of the H-8 proton and of 2"- and 6"-OAc groups are in the 7.25-7.40, 1.77-1.83, and 1.98-2.04 ppm regions [6-9]). The β configuration of the glycosidic bond was confirmed by the presence in the PMR spectrum of (I) of a doublet at 4.87 ppm with a spin–spin coupling constant J = 10 Hz [6-8].

The presence of an ester bond was confirmed by the IR and PMR spectra. The IR spectrum contained an absorption band at 1732 cm^{-1}. The PMR spectrum of compound (I) included a three-proton singlet at 1.74 ppm. In the IR and PMR spectra of (II) both these characteristics were absent. In all its indices (melting point, R_f values, UV, IR, and PMR spectra) the intermediate product (II) corresponded to orientin, which has been isolated from this plant.

The question of the nature of the acyl radical was solved on the basis of the PMR spectrum, a comparative analysis of the acetates of (I) and of orientin, and a chromatographic analysis of the hydrolysis products of the compound under investigation. The PMR spectrum lacked any signals of aromatic protons other than the signals of the flavone protons. In its melting point, a mixed melting point, its R_f values, and its IR and PMR spectra, the full acetate of (I) was identical with orientin octaacetate. When compound (I) was subject to acid and alkaline hydrolysis, no phenolic carboxylic acids were detected in the hydrolyzates. In order to confirm the presence of acetic acid in the molecule of (I) we obtained and identified its hydroxamate [10] and its diethylammonium salt [11-13]. In parallel, we performed the hydroxylaminolysis of ethyl acetate and obtained the diethylammonium salt of free acetic acid.

The problem of determining the position of attachment of the acetyl residue in the molecule was solved on the basis of the PMR spectrum of (I) and of its full acetate. The UV and

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