COUMARINS OF FERULA PENNINERVIS

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Ferula penninervis Rgl. et Schmalh. is a perennial herbaceous plant of the family Umbelliferae which grows in the hot regions of Central Asia. We have studied the coumarins of the roots of Ferula penninervis collected by P. S. Massagetov in 1960 in the spurs of the Tyan'-Shan.

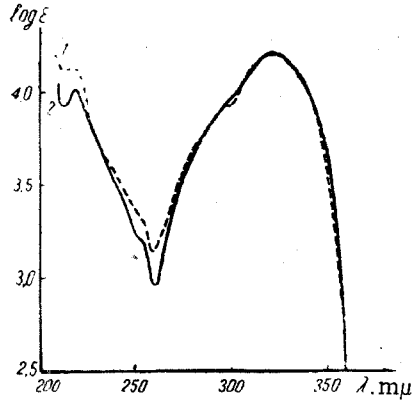


Fig. 1. UV spectra in 96% ethanol. 1) Kamolone; 2) kamolol.

By extraction with methanol followed by chromatographic separation on alumina we isolated three coumarin derivatives: the known umbelliferone, a compound $C_{24}H_{30}O_4$ which has not been described in the literature and is apparently new, which we have called kamolone (from kamol, the local name of the ferula) and a second new substance $C_{24}H_{32}O_2$, kamolol.

The UV spectrum of kamolone (Fig. 1) shows that it belongs to the coumarin group [1]. The IR spectrum (Fig. 2a) shows the presence of a coumarin skeleton and the absence of hydroxyl groups. In the region of the stretching vibrations of the CO group there are two bands at 1733 and 1713 cm^{-1} which may be explained either by the presence of two carbonyl groups in the molecule or by the splitting of the carbonyl band of the α-pyrone ring [2]. The over-all integral intensity of these bands (in chloroform) was 9.80 ± 0.14 pract. units. We have previously [3] obtained a value of 8.1 pract. units for the over-all intensity of the carbonyl band of coumarins in chloroform. Consequently, the second band has an intensity of 1.70 pract. units, which is characteristic for the CO bands of saturated ketones [4].

The presence of one keto group in the molecule of this coumarin was confirmed by the preparation of an oxime and a dinitrophenylhydrazone. The acid decomposition of kamolone gave umbelliferone. The partial structure of kamolone is shown by formula (I).

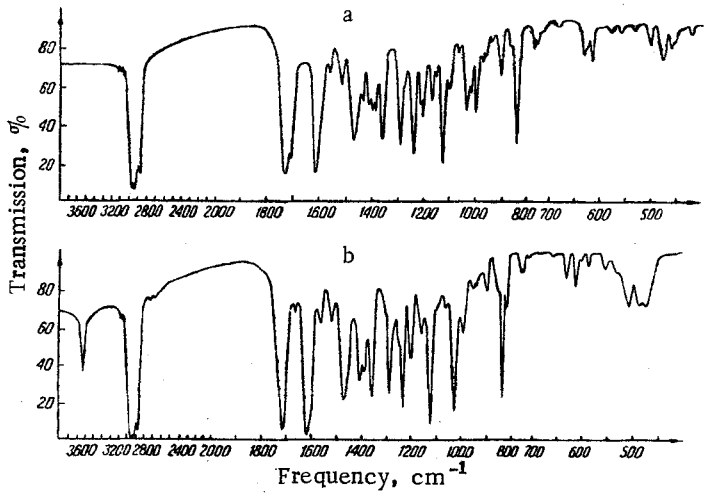


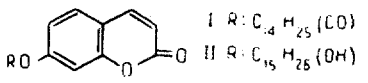
Fig. 2. IR spectra (mull in paraffin oil). a) Kamolone; b) kamolol.

The UV spectrum of kamolol (see Fig. 1) is also typical of coumarins. The IR spectrum of this substance (Fig. 2b) has bands 3525 (alcoholic hydroxyl), 1715 (CO group of an α-pyrone ring), 1613, 1569, and 1516 cm^{-1} (vibrations of benzene and α-pyrone rings).

The presence of one alcoholic hydroxyl in the kamolol molecule was confirmed by the preparation of its mono-

acetate $C_{26}H_{34}O_5$, in whose IR spectrum, as was to be expected, the band of the hydroxyl group is absent and the carbonyl bands of the α-pyrone ring and the acetyl group are superposed on one another, giving a strong maximum at 1730 cm^{-1}.

The acid decomposition of kamolol again gives umbelliferone. Consequently kamolol is a derivative of umbelliferone and a sesquiterpene residue $C_{15}H_{27}O$ (II).



Experimental

The IR spectra were obtained on a UR-10 spectrophotometer, and the UV spectra on a SF-4 spectrophotometer. The substances were investigated in the form of paraffin mulls. Ethanol was used as solvent. The integral intensity of the CO band was calculated by the Wilson-Wells method described by Ramsay [5].

Chromatography was carried out by the descending method on paper impregnated with a 20% solution of formamide in methanol; the mobile phase was petroleum ether–benzene–methanol (5:4:1). The spots were revealed by means of diazotized sulphanilamide [6]. Thin-layer chromatography was carried out on plates with unsupported alumina in the benzene–butyl acetate (2:1) system. The position of the spots was determined by illumination in UV light.

Isolation of umbelliferone. Three kilograms of the comminuted roots was extracted twice with 30-*l* portions of methanol. The extract was concentrated to 3 *l*, 6 *l* of water was added, and the mixture was shaken with 6 *l* of ether. The ethereal extracts, after concentration to 2 *l*, were treated with a 0.5% solution of caustic potash.

The solution was acidified with 20% sulfuric acid and extracted with ether. This gave 61 g of a dark mass, which was dissolved in 300 ml of a 15% solution of sodium carbonate and this was treated with three 100-ml portions of ether. The sodium carbonate solution was acidified with 20% sulfuric acid and extracted with chloroform. After the solvent had been distilled off, 28 g of a resinous mass remained.

A part of the resin obtained (5 g) was chromatographed on a column containing 120 g of inactivated alumina. It was eluted with benzene. When the 3rd–8th fractions were concentrated, they yielded grayish crystals whose solution in alkali fluoresced strongly. After vacuum sublimation (~ 0.05 mm Hg) at 200° C, the substance had mp 228°–230° C.

Found, %: C 66.66, 66.56; H 3.86, 3.85. Calculated for $C_9H_6O_3$, %: C 66.66; H 3.70.

A direct comparison of this substance with umbelliferone showed their identity.

Isolation of kamolone. After the treatment with 0.5% caustic potash solution, the ethereal extract (2 *l*) was washed with water and dried with anhydrous sodium sulfate, and the solvent was distilled off. This yielded 337 g (11.2%) of an orange resin which was dissolved in 200 ml of chloroform and chromatographed on a column of alumina (3 kg, acidic, Brockmann activity grade II, 90 × 6.5 cm). Elution was effected successively with petroleum ether (fractions 1–10), a mixture of petroleum ether and ether [(2:1) for fractions 11–17; (3:2) for fractions 18–20; (1:1) for fractions 21–22], ether (for fractions 23–27), a mixture of chloroform and methanol (1:1) for fractions 28–30, and methanol for fractions 31–33. The volume of each fraction was 500–1000 ml. Coumarin derivatives were found mainly in fractions 11–17 and 23–27.

From fractions 11–17 was isolated 50 g of a yellow crystallizing resin. Eight grams of kamolone (fine needles) with mp 191°–192° C (from ethanol), $[\alpha]_D^{18}$ + 55° (c 1.00; chloroform) was obtained. The substance is readily soluble in chloroform, acetone, ethyl acetate, ether, benzene, pyridine, and alcoholic alkali, is less readily soluble in alcohols, and is insoluble in petroleum ether and water. R_f 0.72 (Al_2O_3/II), R_f 0.93 ("B" paper). UV spectrum: λ_{max} 218, 255 (inflection), 300 (inflection), 324 mμ (log ε 4.22, 3.38, 4.09, 4.29. IR spectrum: 3110, 3080, 3055, 1733, 1713, 1617, 1562, 1518 cm^{-1}.

Found, %: C 75.58, 75.37; H 7.99, 7.93; mol. wt. 363 (Rast), 384 (spectrophotometry). Calculated for $C_{24}H_{30}O_4$, %: C 75.36; H 7.91; mol. wt. 382.5.

Kamolone oxime. A mixture of 0.2 g of kamolone, 0.2 g of hydroxylamine hydrochloride, 1 ml of absolute alcohol and 1 ml of pyridine was heated on a boiling water bath for 2 hr. After the solvent had been eliminated, the residue was recrystallized from ethanol. A sample for analysis was dried in vacuum at 80° C for 2 days; mp 220°–222° C. IR spectrum: 3505, 3090, 1708, 1700 (inflection), 1610, 1560, 1518 cm^{-1}.

Found, %: C 72.87, 72.95; H 7.85, 8.03; N 3.55, 3.57. Calculated for $C_{24}H_{31}O_4N$, %: C 72.52; H 7.86; N 3.52.

Kamolone 2,4-dinitrophenylhydrazone. A solution of 200 mg of the substance in 10 ml of alcohol was treated with an alcoholic solution of the same amount of 2,4-dinitrophenylhydrazine. The dark orange precipitate that was deposited was separated off, dissolved in a small amount of chloroform, and chromatographed on a column containing 20 g of alumina (neutral, activity grade II). When the chloroform eluate was concentrated, a crystalline precipitate was deposited, which was washed with alcohol. The 2,4-dinitrophenylhydrazone is readily soluble in chloroform, and sparingly in alcohol, benzene, ether, and ethyl acetate, mp 250.5°–251.5° C. A sample for analysis was dried at 120° C in vacuum for 6 hr.

Found, %: C 63.94, 63.99; H 6.18, 6.10; N 9.83. Calculated for $C_{30}H_{34}O_7N_4$, %: C 63.98; H 6.09; N 9.99.

Acid decomposition of kamolone. Two drops of concentrated sulfuric acid was added to 100 mg of the substance in 2 ml of glacial acetic acid, and the mixture was heated for 1 hr. Then it was diluted with water and the umbelliferone was extracted with ether. This gave yellowish needles with mp 228°–230° C (from water).

Isolation of kamolol. The residue after the solvent had been distilled off from fractions 23–27 (92 g) was crystallized from ethyl acetate (yield 37 g) and was then recrystallized from a mixture of ethyl acetate and petroleum ether or ether and petroleum ether. This gave short needles or prisms, readily soluble in alcohols, ethyl acetate, chloroform, acetone, and benzene, more sparingly soluble in ether, and insoluble in petroleum ether and water. R_f 0.4 (TLC), R_f 0.75 ("B" paper). UV spectrum: λ_{max} 218, 255, (inflection), 305 (inflection), 324 mμ (log ε 4.02, 3.24, 4.04, 4.29. IR spectrum: 3525, 3080, 3060, 1715, 1613, 1569, 1516 cm^{-1}.

Found, %: C 74.92, 75.12; H 8.31, 8.42; mol. wt. 390 (spectrophotometry). Calculated for $C_{24}H_{32}O_4$, %: C 74.97; H 8.39; mol. wt. 384.5.

Kamolol monoacetate. 0.2 g of kamolol was heated with 2 ml of a mixture of acetic anhydride and pyridine (1:1) on a boiling water bath for 2 hr. After the solvent had been eliminated in vacuum, 0.2 g of residue was obtained and this was recrystallized from 95% alcohol. Short white needles, readily soluble in ether, chloroform, and alcohol. For analysis the substance was dried in vacuum at 80° C for 2 days, mp 155°–156° C. IR spectrum: 3100, 3080, 1730, 1612, 1585 (inflection), 1560, 1519 cm^{-1}.

Found, %: C 73.29, 73.19; H 8.11, 8.08. Calculated for $C_{26}H_{34}O_5$, %: C 73.23; H 8.03.

Acid hydrolysis of kamolol. With stirring, 10 drops of concentrated sulfuric acid was added to a solution of 500 mg of kamolol in 10 ml of glacial acetic acid. The mixture was boiled for 1 hr and was then diluted with 25 ml of water and extracted with ether (5 × 25 ml). The extract was washed with water and dried, and the solvent was distilled off. This gave 0.4 g of a brown residue, from which a crystalline substance with mp 228°–230° C (after vacuum sublimation) was isolated by chromatography on a column of alumina; this was identified by its IR spectrum and a mixed melting point as umbelliferone.

Summary

From the roots of Ferula penninervis Rgl. et Schmalh. have been isolated umbelliferone (7-hydroxycoumarin) and two new coumarins: a ketone with the composition $C_{24}H_{30}O_4$, mp 191°–192° C and an alcohol $C_{24}H_{32}O_4$, mp 141°–142° C, which have been named kamolone and kamolol, respectively.

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