TERPENOID COUMARINS OF *Ferula kokanica*

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From an alcoholic extract of the roots of *Ferula kokanica* Rgl. et Schmalh., collected in the region of the village of Oman-kutan (Samarkand Province), have been isolated polyanthinin, mogoltadone, gummosin, kellerin, feshurin, and umbelliferone, and two new coumarins: deacetylkellerin, $C_{24}H_{32}O_5$, M^+ 400, mp 134-136°C, $[\alpha]_D^{22}$ +52° (c 0.1, ethanol), and kokanidin, $C_{26}H_{34}O_6$, M^+ 442, mp 189-191°C, $[\alpha]_D^{18}$ −30° (c 1.0; ethanol). The structure of deacetylkellerin has been established on the basis of the results of a study of UV, IR, PMR, and mass spectra. The structure and configuration of kokanidin have been established on the basis of spectral characteristics and also conversion into conferol acetate and feshurin.

Kokanikin and galbanic acid have previously been isolated from the roots of *Ferula kokanica* Rgl. et Schmalh. collected in the neighborhood of Dushanbe [1, 2]. As a result of the chromatographic separation of the combined extractive substances of the roots of this plant collected in the region of the village of Oman-kutan (Samarkand Province), we have isolated coumarins identified as polyanthinin [3, 4], mogoltadone [5], gummosin [6, 7], kellerin [8-10], feshurin [11, 12], umbilliferone [13], and two new substances, (I) and (II).

Substance (I), with the composition $C_{24}H_{32}O_5$, M^+ 442, mp 134-136°C, $[\alpha]_D^{22}$ +52° (c 0.1 ethanol) is, according to its UV spectrum [λ_{max} 218, 244, 253, 296, 328 nm (log ε 3.47, 3.0, 2.85, 3.18, 3.41, respectively), an umbelliferone derivative. Its IR spectrum has absorption bands at (cm^{-1}), 3475 (—OH), 1730 (C=O of an α-pyrone), 1618, 1557, and 1513 (aromatic nucleus).

By a comparison of spectral characteristics and also by means of a mixed melting point, (I) was identified as deacetylkellerin [8-10], which has been obtained previously by the saponification of kellerin.

Substance (II), which has been called kokanidin, is an optically active compound, $[\alpha]_D^{18}$ −30° (c 1.0; ethanol), composition $C_{26}H_{34}O_6$, M^+ 442, mp 189-191°C. The IR spectrum of (II) has absorption bands at (cm^{-1}) 3557 (OH group), 1725 and 1716 (C=O of an α-pyrone and of an ester group), and 1620, 1556, and 1515 (aromatic nucleus).

In the strong-field region, the PMR spectrum of (II) contains singlets at 0.86, 0.91, and 1.09 ppm (3 H each) from methyl groups attached to quaternary carbon atoms and a singlet at 1.24 ppm (3 H) of a methyl group at C_2'. Then in 2.03 ppm region is observed the singlet signal (3 H) of the methyl group of an acetyl residue. The methyl protons of R—O—CH_2—CH grouping appear in the form of two quartets at 4.11 ppm (1 H) with J_{gem} = 10 Hz, J_{vic} = 3 Hz and at 4.32 ppm (1 H) with J_{gem} = 10 Hz, J_{vic} = 4 Hz. The signal of the geminal proton is observed in the form of a broadened singlet (1 H) at 4.60 ppm with a half-width of 7 Hz. In the 6.21-7.33 ppm region are observed signals due to the protons of a 7-hydroxy-substituted coumarin nucleus at (ppm) 6.17, d, 1 H, $J_{3,4}$ = 9.5 Hz (H_3); 7.60, d, 1 H, $J_{4,3}$ = 9.5 Hz (H_4); 6.71, m, 2 H (H_6 and H_8); and 7.33, d, 1 H, $J_{5,6}$ = 9.0 Hz (H_5).

Consequently, according to its composition and spectral characteristics, kokanidin is an ether of 7-hydroxycoumarin and an iresane sesquiterpene alcohol in which there is a hydroxyl at C_2' and an acetyl residue at C_6' and for which it is possible to put forward structure (II). It remained to determine the configuration of (II), and this was established in the following way. From the multiplicity of the signal of the geminal proton ($W_{1/2}$ = 7 Hz) it is possible to judge that it is present in the equatorial orientation and, consequently, the acetyl residue has the axial orientation. The configuration of C_2' in kokanidin was established by comparing the PMR spectra of samarcandin acetate [14] and of kokanidin.

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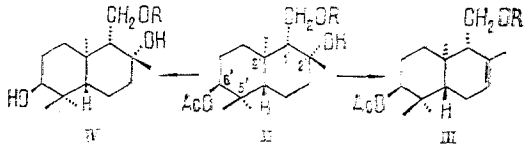
In the spectrum of samarcandin acetate there is the signal of only one methyl group below 1 ppm (at 1.18 ppm), and this must be assigned to the C_2'—CH_3 group, while in the case of kokanidin there are two methyl groups giving signals below 1 ppm (at 1.24 and 1.09 ppm), one of which relates to a C_2'—CH_3 and the other to a C_9'—CH_3 group. This phenomenon is explained in the following way. The 1,3-diaxial interaction of the tertiary hydroxyl and the angular methyl group exert a descreening influence on the methyl group and the signal of the latter is shifted downfield.

The orientation of the C_1'—CH_2—OR section was determined from the results of the dehydration of (II). The product of this process was identified as conferol acetate (III) (R = coumarin-7-yl) [15].



Thus, in kokanidin the tertiary hydroxy group is present in the axial orientation and the —CH_2—OR substituent in the equatorial orientation, and configuration (II) is proposed for it.

The alkaline hydrolysis of (II) gave a de-acetate which proved to be identical with feshurin (IV) [11, 12]. It must be mentioned that a configuration with the equatorial orientation of the hydroxyl at C_2' has been proposed previously for feshurin [12]. This configuration is not in harmony with the more recent results based on the PMR spectrum of kokanidin. Consequently, in feshurin (IV), just as in kokanidin, the tertiary hydroxy group has the axial orientation.

On the basis of the results given above, it may be concluded that kokanidin has the structure and configuration (II), and feshurin the structure and configuration (IV). It has also been shown that the *F. kokanica* collected in Oman-kutan differs in its chemical composition from the plant collected close to Dushanbe.

EXPERIMENTAL

The conditions for taking the spectra have been described previously [10]. For chromatography we used type KSK silica gel. The homogeneity of the substances and the course of the reactions were monitored by TLC on Silufol plates in the chloroform—ethyl acetate (3:1) system.

Isolation of the Combined Coumarins. The comminuted roots (2.5 kg) were extracted with ethanol three times, using 8-, 5-, and 5-liter portions, for 17 h each time. After the solvent had been eliminated in vacuum, 240 g of a crude resinous residue was obtained. The crude extract was diluted with water (1:2) and treated with diethyl ether. The ethereal extract was treated with a 1% solution of KOH and was then washed with water to neutrality and dried, and the solvent was distilled off. This gave 190 g (7.6%) of combined neutral substances.

Separation of the Coumarins. The neutral extract (130 g) was chromatographed on a column (5.5 × 40 cm) of silica gel L 50/100 μm (600 g). As the eluant we used hexane—ethyl acetate (4:1) and mixtures of the same solvents with increasing concentrations of ethyl acetate. Fractions with a volume of 300 ml each were collected.

Polyanthinin. Fractions 6-9 [eluent hexane—ethyl acetate (4:1)] yielded 25 g (1%) of a crystalline substance ($C_{26}H_{32}O_5$, M^+ 424, mp 127-129°C, R_f 0.72).

Mogoltadone. Fractions 17-19 [eluent hexane—ethyl acetate (4:1)] yield 2.5 g (0.1%) of a coumarin $C_{24}H_{28}O_4$, M^+ 380, mp 132-133°C, R_f 0.70.

Gummosin. When fractions 20-35 [eluent hexane—ethyl acetate (2:1)] were concentrated, 15 g (0.6%) of a crystalline compound $C_{24}H_{30}O_4$, M^+ 382, mp 176-177°C, R_f 0.36, was obtained.

Kokanidin (II). The residue from the mother liquor (after the crystallization of gummosin) (4 g) was chromatographed on a column (1.5 × 150 cm) of silica gel in the hexane—ethyl acetate (4:1) system. Fractions 28-34 yielded 2.5 g (0.1%) of a substance with the composition $C_{26}H_{34}O_6$, M^+ 442, mp 189-191°C, $[\alpha]_D^{18}$ −30° (c, 1.0; ethanol). UV spectrum, $\lambda_{max}^{ethanol}$, nm: 219, 244, 254, 295, 327 (log ε 4.21; 3.75; 3.61; 3.96; 4.21), R_f 0.46.

Kellerin. After the solvent had been distilled off from fractions 36-44 [eluent hexane–ethyl acetate (1:1)], 8 g (0.22%) of a substance $C_{26}H_{34}O_6$ with M^+ 442, mp 76-78°C, R_f 0.27, was isolated.

Feshurin. Fractions 50-55 yielded 1.0 g (0.04%) of a crystalline compound with the composition $C_{24}H_{32}O_5$, M^+ 400, mp 213-215°C, $\alpha[]_D^{18}$ −180° (c 0.1; pyridine), R_f 0.17.

De-acetylkellerin (I). Fractions 58-60 [eluant hexane–ethyl acetate (4:1)] yielded 0.5 g (0.02%) of a coumarin $C_{24}H_{32}O_5$, M^+ 400, mp 134-136°C, $[\alpha]_D^{22}$ +52°, (c 0.1; ethanol), R_f 0.27.

Umbelliferone. From a concentrated extract of fractions 66-71 [eluant hexane–ethyl acetate (1:2)], crystals deposited with the composition $C_9H_6O_3$, M^+ 162, mp 233-234°C, R_f 0.37.

Dehydration of Kokanidin (II). A solution of 0.1 g of kokanidin (II) in 20 ml of anhydrous acetone containing 4% of sulfuric acid was heated for 30 min. After cooling, it was treated with ether. The ethereal extract was washed with water and the solvent was distilled off. After crystallization from diethyl ether–hexane, 0.06 g of conferol acetate (III) [15], $C_{24}H_{32}O_5$, M^+ 424, mp 159-160°C, $[\alpha]_D^{20}$ −42.39° (c 0.9; $CHCl_3$) was obtained

Saponification of Kokanidin (II). A solution of 0.25 g of (II) in 15 ml of 5% aqueous alcoholic caustic potash was heated on the water bath for 2 h. After working up, 1.18 g of feshurin (IV) with mp 213-215°C was obtained.

SUMMARY

Polyanthinin, mogoltadone, gummosin, kellerin, feshurin, deacetylkellerin, and a new coumarin, kokanidin, have been isolated from the roots of *Ferula kokanica* Rgl. et Schmalh.

On the basis of a study of chemical properties and spectral characteristics, the structure and configuration of kokanidin have been established, and the configuration of feshurin has been refined.

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