STRUCTURE AND CONFIGURATION OF NEW COUMARINS OF THE ROOTS OF Ferula mogoltavica

T. Kh. Khasanov, A. I. Saidkhodzhaev, and G. K. Nikonov

UDC 547.587

Three isomeric coumarins – samarcandin (I), isosamarcandin (II), and nevskin (III) [1-3] – differing in the orientation of the substituents at C_3 and C_9 of the decalin nucleus have previously been isolated from plants of the genus Ferula.

In a study of the coumarins of the roots of Ferula mogoltavica collected in 1972 in the village of Chashma (Leninabad oblast, Tadzhik SSR) we have isolated gummosin (V), mogoltavicin (VI), and a fourth isomeric coumarin with the composition $C_{24}H_{32}O_5$ (M^+ 400), mp 159-161°C, $[\alpha]_D^{23}-16°$ (c 1.1; ethanol) which we have called mogoltavidin (IV). The UV spectrum of (IV) has maxima at 218, 245, 254, and 327 nm (log ε 4.11, 3.60, 3.50, and 4.17), showing the presence in it of the chromophore of 7-hydroxycoumarin, and in the IR spectrum (Fig. 1) there are absorption bands at (cm^{-1}) 3400-3600 (hydroxy group), 1720 (lactone carbonyl), 1670, 1620, and 1560 (aromatic nucleus). The mass spectrum of (IV) has the peaks of ions with m/e 400 (M^+), 382 $(M-H_2O)^+$, 221 $(M-RD-H_2O)^+$, 220 $(M-ROH-H_2O)^+$, 203 $(M-RO-2H_2O)^+$ with relative intensities of 1, 7, 14, 3, and 100%, respectively.

In the NMR spectrum of (IV), the protons of the coumarin nucleus appear at 6.08 and 7.48 ppm (J = 10.5 Hz, d, 1 H each, C_3-H and C_4-H), 6.75 ppm (s, 1 H, C_8-H), 6.65 ppm (q, 1 H, J_1 = 6 Hz, J_2 = 2 Hz; C_6-H), and 7.25 ppm (d, 1 H, J = 7 Hz, C_5-H). Singlets at 0.9 and at 0.78 and 0.9 ppm (3 H each) relate to the methyl group at C_{10} and those at C_4, respectively, and a singlet at 1.16 ppm corresponds to a methyl group in the geminal position to a tertiary hydroxy group (C_8-CH_3). A broadened singlet at 2.17 ppm (2 H) is due to the protons of a hydroxy group, and two quartets at 4.00 ppm and 4.05 ppm with a total intensity of two proton units (J_1 = 10.5 Hz; J_2 = 4 Hz; J_1 = 10.5 Hz, J_2 = 4 Hz) are due to an $ArOCH_2-$ grouping.

The presence of the signal of a methine proton geminal to a hydroxy group at 3.28 ppm that undergoes a paramagnetic shift of 70 Hz in the spectrum of the acetate and its multiplicity (t, $^1/_2 \Sigma$ 5 Hz) shows that the other hydroxy group is secondary and is located at C_1 or C_3. The choice between these alternative structures was made on the basis of the chemical shifts (CSs) of the methyl groups in the NMR spectrum of samarcandin and mogoltavidin, their acetates, and their dehydrogenation products. In the spectra of samarcandin and mogoltavidin, the signals of the angular methyl groups are located at 0.78 and 0.90 ppm, and in

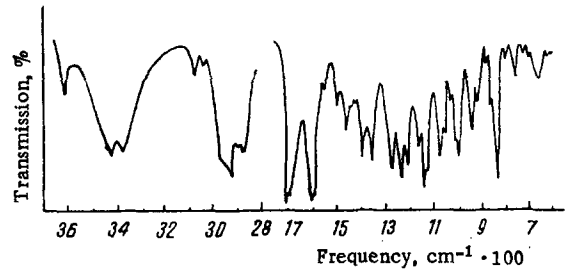


Fig. 1. IR spectrum (KBr) of mogoltavidin.

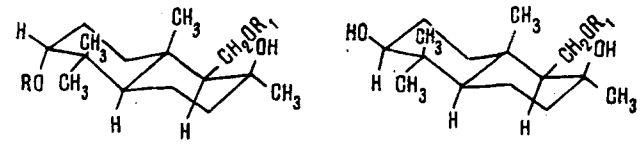
Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 10-14, January-February, 1974. Original article submitted July 5, 1972.

TABLE 1. CS Values (δ scale)

Substance	$C_{10}-CH_3$, 3H	C_4-2CH_3, 6H	C_8-CH_3, 3H
Samarcandin (I)	0,78	0,80 0,89	1,18
Samarcandin acetate (Ia)	0,80	0,80 0,86	1,18
Mogoltavidin (IV)	0,90	0,78 0,9	1,26
Mogoltavidin acetate (IVa)	0,91	0,80 0,86	1,16

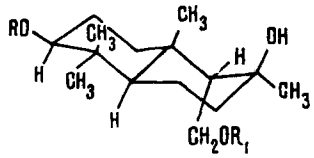
their acetates they are at 0.80 and 0.91 ppm, respectively (Table 1). The difference of 0.12 ppm is due to the position of the substituent at C_9 in the axial or the equatorial position [1, 4, 5]. The dehydrogenation of (IV) with selenium gave 1,2,5,6-tetramethylnaphthalene which could be formed only if there was a hydroxy group at C_3. Consequently, a hydroxy group is located at C_3.

On the basis of these results, mogoltavidin has the structure (IV). A comparison of the CS's of the methyl and methine protons of (I) and (IV) enables us to establish that mogoltavidin is a fourth geometric isomer of samarcandin (the configurations of samarcandin and nevskin have been established previously [2], and the configuration of isosamarcandin is proposed by us). This is confirmed by the mass spectra of mogoltavidin, samarcandin, and nevskin. Thus, for example, the relative intensities of the peaks with m/e 400, 382, 221, 220, and 203 in the spectrum of samarcandin are 5, 3, 30, 36, and 49%; in nevskin they are 16, 1, 6, 4, and 18%; and in mogoltavidin 1, 7, 14, 3, and 100%, respectively. The change in the relative intensities of the main fragments in the mass spectrometry of (I), (III), and (IV) shows that they are isomeric compounds [7].

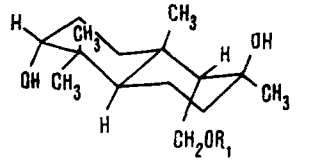


I

II



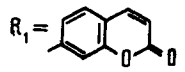
III



IV

I – IV R=H

Ia–IVa R=Ac



The results of a comparison of the CS's of the angular methyl groups in the NMR spectra of (I) and (IV) and their acetates (Ia, IVa) show that the axial orientation of the substituent at C_9 ($-CH_2OAr$), i.e., its trans position with respect to the angular methyl group at C_{10} is responsible for the position of the signal of this group in the weaker field at 0.9 ppm.

When the same substituent is present in the equatorial orientation, i.e., in the cis position, the screening effect is enhanced, and the signal is observed in the stronger field at 0.78-0.8 ppm. On this basis, in (I) the substituent at C_9 has the equatorial orientation and in (IV), the axial orientation.

The hydroxy group at C_3, regardless of its orientation, also has an influence on the methyl group at C_{10}, but a very slight one (0.03 ppm) [4, 5]. The configuration of the hydroxy group at C_3 in (IV) was established on the basis of the CSs and the half-widths of the signal of the methine protons in the NMR spectra of (IV) and (IVa). In the spectrum of (IV), the signal of the methine proton is found at 3.28 ppm ($^1/_2\ \Sigma = 5$ Hz) and in (IVa) at 4.42 ppm ($^1/_2\ \Sigma = 5$ Hz). The value of the half-widths shows that the methine proton at (IV) is present in the equatorial position and interacts with the axial and equatorial protons at C_2. Hence, the hydroxy group at C_3 has the axial orientation.

Consequently, mogoltavidin has the structure and configuration (IV). The correctness of the proposed structure was confirmed by passage from mogoltavidin to nevskin.

The oxidation of (IV) with chromium trioxide in acetone gave a ketone $C_{24}H_{30}O_5$. The reduction of mogoltavidone with sodium tetrahydroborate led to nevskin, $C_{24}H_{32}O_5$, mp 189-190°C, in the NMR spectrum of which the half-width of the signal of the proton geminal to the hydroxy group at C_3 was 16 Hz, which shows the equatorial orientation of the hydroxy group.

Gummosin – substance (V) with the composition $C_{24}H_{30}O_5$, mp 177-178°C, $[\alpha]_D^{23}-39°$ (c 1.2; ethanol). Its IR spectrum had absorption bands at (cm^{-1}) 3500-3600 (hydroxy group), 1720 (lactone carbonyl), and 1660, 1620, and 1580 (aromatic nucleus). From its IR spectrum, specific rotation, and melting point of a mixture with an authentic sample of gummosin which we isolated from Ferula samarcandica, substance (V) is identical with gummosin.

Mogoltavicin – substance (VI) with the composition $C_{26}H_{34}O_6$, mp 151-152°C, $[\alpha]_D^{23}-12°$ (c 1.2; ethanol). Its IR spectrum shows absorption bands at (cm^{-1}) 3400-3500 (hydroxy group), 1735 (ester C = O), and 1720 (lactone C = O). The hydrolysis of (VI) with 5% alkali gave mogoltavidin (IV) and acetic acid which were identified, respectively, by a mixed melting point and by paper chromatography.

In the NMR spectrum of (VI) there is a one-proton broadened singlet at 4.45 ppm ($^1/_2\ \Sigma$ = 5 Hz) relating to a proton geminal to an ester grouping. This shows that mogoltavidin is esterified by acetic acid at the secondary hydroxy group (on C_3).

On this basis, it has been established that substance (VI) is a natural acetate of mogoltavidin; the structure and configuration (IVa) are proposed for it.

EXPERIMENTAL

The conditions for recording the spectra have been described previously [8]. The results of the elementary analyses corresponded to calculated figures.

Isolation of Mogoltavidin (IV) and Gummosin (V). A methanolic extract of the roots of Ferula mogoltavica (20 g) was separated on a column (h = 30 cm, d = 6 cm) filled with type KSK silica gel (size 0.25 mm).

On elution with petroleum ether–ethyl acetate (1 : 3), fractions 10-16 yielded gummosin with mp 177-178°C, and fractions 24-31 yielded mogoltavidin with mp 160-162°C.

Mogoltavidin Acetate (IVa). A solution of 0.07 g of mogoltavidin in 3 ml of pyridine was treated with 2 ml of acetic anhydride and the mixture was heated at 80°C for 4 h. Mogoltavidin acetate was obtained in the usual way. Mp 151-152°C.

The Ketone from Mogoltavidin. A solution of 0.1 g of chromium trioxide in 5 ml of water was added to 0.2 g of mogoltavidin in 15 ml of acetone. After 2 h, the mixture was diluted with water and the ketone formed – mogoltavidone – was extracted with ether. Mp 226-227°C (from ether).

Reduction of Mogoltavidone with Sodium Tetrahydroborate. A solution of 0.12 g of the ketone in 30 ml of 85% aqueous methanol was treated with 0.2 g of sodium tetrahydroborate. After 6 h, the reaction product was isolated in the usual way. Mp 189-190°C (from ether).

Samarcandone. A solution of 0.2 g of chromium trioxide in 6 ml of 80% acetic acid was added to 0.2 g of samarcandin, which we had isolated from F. samarcandica in 5 ml of glacial acetic acid, and the mixture was left at room temperature for 2 h. After dilution with water (1 : 2), the samarcandone was extracted with ether. Mp 212-213°C (from ethanol).

The IR spectrum lacked the absorption band of a carbonyl group.

Isosamarcandin Acetate (IIa). Obtained by the method given for (IVa). Mp 210-212°C.

Isolation of Mogoltavicin (VI). A methanolic extract of the roots (10 g) was separated on a column of silica gel (h = 30, d = 6 cm). On elution with benzene, fractions 6-9 yielded substance (VI) with mp 151-152°C.

Saponification of Substance (VI). A solution of 0.1 g of the substance in 15 ml of 5% aqueous caustic potash was heated for 2 h. From the hydrolysis products mogoltavidin was obtained with mp 159-161°C. Acetic acid was identified by the usual method, R_f 0.13 (solvent system: butanol saturated with 1.5 N ammonia).

CONCLUSIONS

From the roots of Ferula mogoltavica, two new terpenoid coumarins have been isolated – mogoltavidin and mogoltavicin – and also one known one – gummosin.

On the basis of a comparison of the spectra of mogoltavidin and those of known isomers it has been established that (IV) is the ether of umbelliferone and trans-3,8 dihydroxy-4,4,8,10-tetramethyldecalin-9-yl carbinol with the axial arrangement of the hydroxy groups.

Mogoltavicin is the natural acetyl derivative of mogoltavidin at the secondary hydroxy group.

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