THE STRUCTURE OF MOGOLTIN – A COUMARIN FROM THE ROOTS OF Peucedanum mogoltavicum

G. K. Nikonov

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We have previously [1] reported the isolation from the roots of Peucedanum mogoltavicum Korov. of three new coumarins: mogoltin $C_{24}H_{30}O_5$, mogoltavin $C_{27}H_{34}O_6$, and mogoltavinin $C_{29}H_{36}O_6$. As shown by the products of acid cleavage, these lactones are ethers of umbelliferone and sesquiterpene alcohols. We have continued our study of these coumarins using spectroscopic methods. In the present paper we give the results of a study of mogoltin, $C_{24}H_{30}O_5$, mp 183-185°C, $[\alpha]^{22}_{D}$ −63.3° (chloroform).

As follows from the empirical formula, the composition of the terpenoid moiety of mogoltin is $C_{15}H_{25}O_2$; it contains one hydrogenatable double bond, which is confirmed by the production of a dihydro derivative $C_{24}H_{32}O_5$ with mp 107-108°C and by NMR spectroscopy (see below). Both oxygen atoms are present in hydroxy groups (diacetate $C_{28}H_{34}O_7$ with mp 197-198°C). From these considerations it may be concluded that the sesquiterpene moiety of mogoltin cannot have an open chain or a monocyclic structure; it must be bicyclic. This conclusion is in agreement with the fragmentation of the lactone under the influence of electron impact, which is extremely similar to that for a lactone of the type of kamolone and others [2]. The dehydrogenation of mogoltin with selenium yielded a hydrocarbon $C_{14}H_{16}$, M^+ 184, giving a picrate with mp 148-149°C, which was identified as 1,2,5,6-tetramethylnaphthalene. The formation of the latter permits the assumption that the sesquiterpene moiety is represented by a decalin structure and that one of the hydroxy groups is present in position 6. Because of the retropinacolone rearrangement possible when a hydroxy group is present on a neighboring carbon atom, one of the gem-dimethyl groups at C-5 migrates on dehydrogenation to C-6, as a result of which not 1,2,5-tri- but 1,2,5,6-tetramethylnaphthalene is formed.

The mass spectrum of mogoltin (Fig. 1) contains the peak of the molecular ion with M^+ 398 and a group of high-intensity peaks, among which those with m/e 162 and 163 are probably due to the molecular and protonated ions of umbelliferone and the peak with m/e 237 to the terpenoid moiety of the molecule. Medium-intensity peaks with m/e 175 and 176 are apparently connected with α-cleavage with respect to the oxygen atom of the ether linkage with and without the transfer of hydrogen from the terpene part of the molecule to the coumarin part, and the peaks with m/e 145 and 119 are connected with the products of the subsequent degradation of the coumarin moiety. Mogoltin contains two hydroxy groups [1], and therefore the fragments with m/e 219 and 201 correspond to the successive splitting off of two molecules of water from the terpenoid residue.

The NMR spectrum of mogoltin (Fig. 2) has doublets at 7.59 and 6.20 ppm, J = 10.5 Hz, corresponding to the H-4 and H-3 protons; a quartet at 6.79 ppm, $J_1 = 9.5$, $J_2 = 2.0$ Hz; a doublet at 7.34 ppm, J = 9.5 Hz; and a broadened singlet at 6.83 ppm, due, respectively, to the H-6, H-5, and H-8 protons of the coumarin nucleus [3, 4]. In the strong-field region there are the signals of the gem-dimethyl group on carbon atom 5 – singlets at 1.08 and 0.99 ppm (3H each) – and of the angular methyl group – singlet at 0.91 ppm (3H). In addition to this, the mogoltin molecule contains one methyl group located on a double bond, as is shown by a broadened singlet at 1.67 ppm. The broadening of the latter is caused by long-range allyl interaction of the protons of the methyl group with the olefinic proton, which appears in the form of a multiplet at 5.48 ppm. The half-width of this multiplet is 10 Hz and is somewhat greater than that for a methyl group. Consequently, there is a secondary or tertiary carbon atom in the vicinal position. Judging from the values

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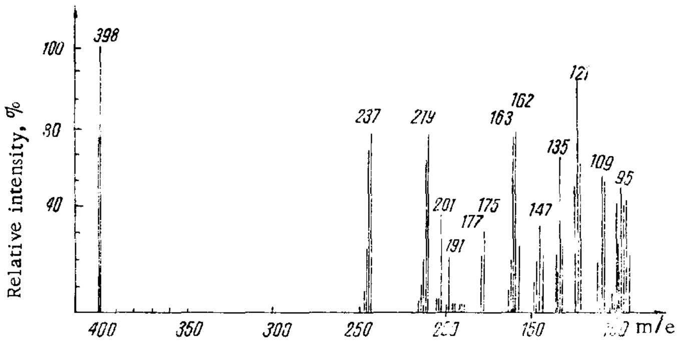


Fig. 1. Mass spectrum of mogoltin.

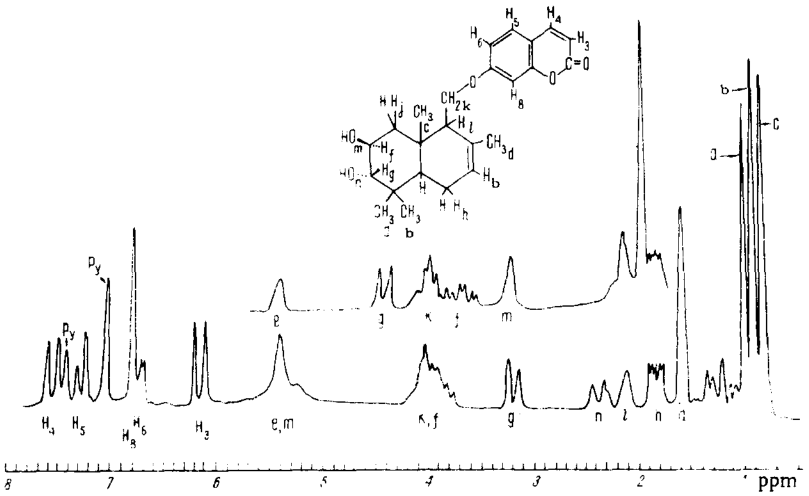
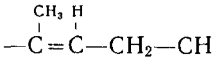
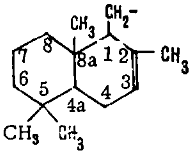


Fig. 2. NMR spectra of mogoltin in deuteropyridine (below) and of mogoltin acetate in deuterochloroform (above).

of the chemical shifts and their integral intensities, the neighboring position is most probably occupied by a methylene group, appearing in the form of a multiplet at 1.97 ppm (2H). These results show that the mogoltin molecule contains the  $-\overset{CH_3}{\overset{|}{C}}=\overset{H}{\overset{|}{C}}-CH_2-CH$ fragment. This is confirmed by a band at 812 cm-1 in the IR spectrum of the lactone, corresponding to a triply substituted C=C group (Fig. 3).

A multiplet at 5.48 ppm possesses an intensity corresponding to two protons, which is due to the superposition of the signals of the olefinic proton and one of the hydroxyl protons. (On deuterium exchange, the intensity of the signal decreases to one unit.) The presence of one double bond in the mogoltin molecule is shown by the production of dihydromogoltin, $C_{24}H_{32}O_5$, M^+ 390, in whose NMR spectrum the signals of the olefinic proton and of the methyl on a double bond have disappeared and a doublet has appeared at 0.82 ppm, J = 8 Hz, corresponding to a methyl group on a secondary carbon atom.

A broadened multiplet in the 3.8-4.3 ppm region (3H) is due to the methylene protons in an $Ar-OCH_2-$ grouping, and its increased intensity to the superposition on it of the signal of a methine proton on a carbon atom to which a hydroxyl is attached. In the NMR spectrum of the monoacetate (see Fig. 2), the methylene protons give a poorly resolved quartet at 4.07 ppm, J = 4.5 Hz (2H), and in the diacetate a well-defined doublet with traces of secondary splitting at 3.98 ppm, $J_1 = 4.5$ and $J_2 = 1.0$ Hz. The splitting of the latter signal shows that there is a methine proton adjacent to the methylene group. As V. Yu. Bagirov et al. have shown by the double-resonance method [5], the signal of the methylene proton in an $ArOCH_2-CH$ grouping is in the region around 1.9 ppm, and in our case it appears in the form of a poorly resolved multiplet at 2.19 ppm (1H). The half-width of the latter is equal to that of the doublet at 3.98 ppm, from which it follows that there is only one methine proton in the vicinal position. The facts presented permit the conclusion that the terpenoid moiety of mogoltin is based on the following skeleton:



The determination of the positions of the two hydroxy groups (at C-4a, C-6, C-7, or C-8) was based on a comparison of the NMR spectra of the initial lactone and its mono- and diacetates. The spectra of the initial lactone showed the signals mentioned above of two methine protons on carbon atoms to which hydroxyls are attached – a doublet at 3.27 ppm, J = 11 Hz, and a triplet with appreciable secondary splitting at 3.78 ppm, $J_1 = 11$ Hz and $J_2 = 4.7$ Hz – and those of two hydroxy groups in the 5.47 and 2.45 ppm regions which disappeared on deuterium exchange. In the monoacetate, the signals of the methine protons are represented by a doublet at 4.58 ppm, J = 11 Hz, and a triplet at 3.78 ppm, $J_1 = 11$ Hz, $J_2 = 4.7$ Hz, while in the diacetate they are represented by a quartet at 4.97 ppm, $J_1 = 11$ Hz, $J_2 = 4.7$ Hz, and a singlet at 4.76 ppm. The existence of the signals of methine protons that have been mentioned exclude the possibility of a hydroxy group at C-4a, while the nature of the spin–spin coupling shows that the hydroxy groups occupy vicinal positions at C-7 and C-8 or at C-6 and C-7. The choice between these structural variants can be made on the basis of the chemical shifts of the signals of the methyl groups at C-8a and C-5 in the spectra of the mogoltin acetates. Because of the electron-accepting influence of an ester carbonyl, in the case of the first variant a paramagnetic shift of the signal of the methyl at C-8a was to be expected, and in the second a similar shift of the gem-dimethyl groups at C-5. The results of a consideration of the NMR spectra of the mono- and diacetates showed that in both cases the signal of the C-5 methyl groups is shifted by 0.08 ppm, which is in favor of the second structure (C_6–OH, C_7–OH).

The spin–spin coupling constant of the H-6 proton (11 Hz) shows its axial position [6]. The nature of the splitting of the signal of the H-7 proton, interacting with two axial protons (H-7 and H-8*a*) and one equatorial proton (H=8e), confirms the axial position of the latter. Thus, both hydroxy groups in the molecule of mogoltin are equatorial (see also the strong absorption bands at 3396 and 1030 cm^{-1} in the IR spectrum). The methylene protons at C-8 appear in the form of a triplet at 1.38 ppm, J = 4.7 Hz (2H), which is characteristic of geminal ring protons interacting with axial protons. The half-width of the signal of the H-7 methine proton at C-7 is equal to that of the sum of the signals of the H-6 and H-8 protons. The positions of the hydroxy groups on vicinal carbon atoms is confirmed by the ready oxidation of mogoltin by lead tetraacetate to an aldehyde, which was obtained in the amorphous state (bands in the IR spectra at 1740-1720, 2870, 2740, 1360, and 1400 cm^{-1}) (see Fig. 3).

On the basis of the results presented, it may be concluded that mogoltin is the ether of umbelliferone and 6,7-dihydroxy-2,5,5,8a-tetramethyl-Δ^2-octahydro-1-naphthylmethanol and has the structure shown in Fig. 2.

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrometer (KBr), the NMR spectra on a JNM-100/100-4H MHz instrument (solutions of the substances in pyridine and deuterochloroform, signals given on the δ scale from the signal of HMDS taken as 0), and the mass spectra on an MKh-1303 instrument fitted with a system for the direct introduction of the substance into the ion source at an ionizing potential of 40 V and a temperature of 180°C. The purity of the substances was checked by chromatography on paper impregnated with a 10% solution of formamide in methanol in the hexane–benzene–methanol (5 : 4 : 1) system.

1,2,5,6-Tetramethylnaphthalene. A mixture of 0.5 g of mogoltin and 5 g of powdered selenium was heated in an oil bath to 250-270°C for 2 h. Then the mixture was cooled and treated with ether (3× 30 ml). The ethereal extract was washed with a 2% solution of caustic potash, dried, and distilled. The residue was dissolved in 10 ml of petroleum ether and passed through a column of Al_2O_3 (12× 2 cm), which was washed with a further 10 ml of the same solvent. The eluate was distilled, the residue was dissolved in 1 ml of ethanol, and 0.5 ml of a 1% ethanolic solution of picric acid was added. After a day, the red crystalline precipitate that had deposited was filtered off. Then it was rechromatographed under the conditions described above. This gave a colorless oily residue with M^+ 184, forming a crystalline picrate with mp 148-149°C corresponding to the adduct of 1,2,5,6-tetramethylnaphthalene.

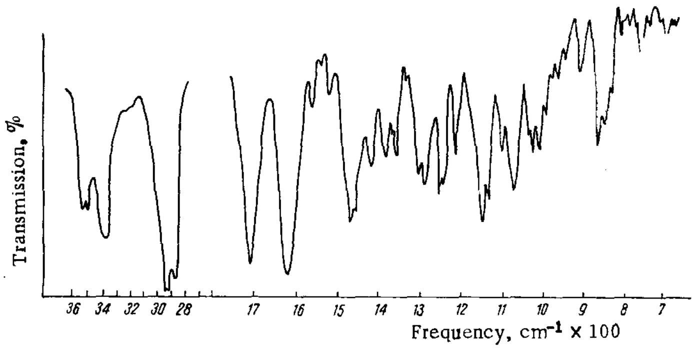


Fig. 3. IR spectrum of mogoltin.

Dihydromogoltin. At room temperature, 0.84 g of the substance in 15 ml of acetic acid was hydrogenated in the presence of 0.05 g of PtO$_2$. About 60 ml of hydrogen was absorbed. The catalyst was filtered off, the filtrate was distilled off in vacuum, and the residue was recrystallized from methanol. A colorless substance with mp 107-108°C, M$^+$ 400, was formed.

Oxidation with Chromium Trioxide. To 0.25 g of the substance in 25 ml of acetone was added 5 ml of Beckmann's mixture, and the resulting mixture was left at room temperature for 10 min. Then the liquid was diluted with 50 ml of water and treated with ether. The extract was distilled and the residue was crystallized from the same solvent. This gave colorless crystals with mp 115°C (decomp.); the 2,4-dinitrophenylhydrazone had mp 137-140°C.

Oxidation with Lead Tetraacetate. To 0.7 g of the substance in 45 ml of chloroform was added 1.5 g of lead tetraacetate, and the mixture was left for a day. Then the liquid was diluted with ether (1 : 1), washed with water, dried, and distilled to give an amorphous substance with R_f 0.90.

SUMMARY

The structure of the coumarin mogoltin isolated previously from the roots of Peucedanum mogoltavicum Korov has been established on the basis of NMR, mass, and IR spectroscopy and the preparation of derivatives. It has been shown that mogoltin is the ether of umbelliferone and 6,7-dihydroxy-2,5,5,8a-tetramethyl-Δ^2-octahydro-1-naphthylmethanol with the equatorial arrangement of the hydroxy groups.

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