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A NEW SESQUITERPENE LACTONE — ALKHANOL FROM *Artemisia fragrans*

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The structure of the new sesquiterpene lactone alkhanol from *Artemisia fragrans* has been studied. On the basis of spectral and chemical characteristics a most probable structure has been suggested for alkhanol.

A sesquiterpene lactone alkhanin isolated from *Artemisia fragrans* Willd. has been reported previously [1]. The present paper gives information on a new sesquiterpene lactone also isolated from this plant which has been called alkhanol.

Alkhanol has the composition $C_{15}H_{22}O_4$, mp 179-181°C. The IR spectrum (Fig. 1) shows, in the region of characteristic frequencies, bands of an OH group (3360 cm^{-1}), of a CO group of a γ-lactone ring (1775, 1760 cm^{-1}), and of a double bond (1665 cm^{-1}). Acetylation led to a diacetyl derivative $C_{19}H_{26}O_6$ with mp 194-196°C, the IR spectrum of which contained the band of the CO group of a γ-lactone ring (1775 cm^{-1}) and the bands of acetyl CO groups (1725, 1270 and 1240 cm^{-1}). There was no band of OH groups in the spectrum. Thus, of the four oxygen atoms of the alkhanol molecule, two form a lactone ring and two are present in two hydroxy groups.

The following signals appeared in the strong field in the NMR spectrum of alkhanol (Fig. 2): a singlet from an angular methyl group at 1.06 ppm ($CH_3-\overset{|}{\underset{|}{C}}-$), a doublet from a secondary methyl group with its center at 1.23 ppm (J = 7 Hz, $CH_3-CH\langle$), a doublet from a vinyl methyl group at 2.04 ppm (J = 2 Hz; 3 H, $CH_3-\overset{|}{C}=$).

One-proton signals at 3.59 and 3.92 ppm belong to two protons in the geminal positions to hydroxy groups. Consequently, these groups are secondary. The fact that these signals are those of hemihydroxylic protons is confirmed by the PMR spectrum of the diacetyl derivative of alkhanol, in which they undergo a paramagnetic shift and appear at 4.62 and 5.16 ppm in the form of a triplet (J = 3 Hz) and an unresolved quartet (J_1 = 3 Hz, J_2 = 6 Hz), respectively. The singlet of the angular methyl group in the spectrum of the diacetate also shifts

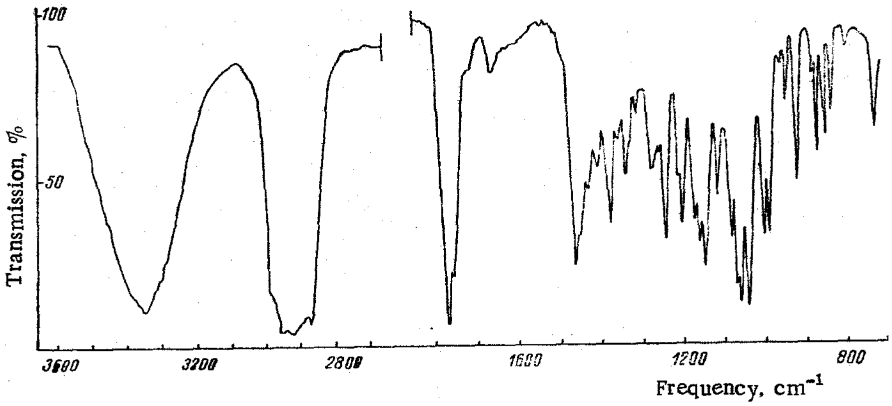

Fig. 1. IR spectrum of alkhanol.

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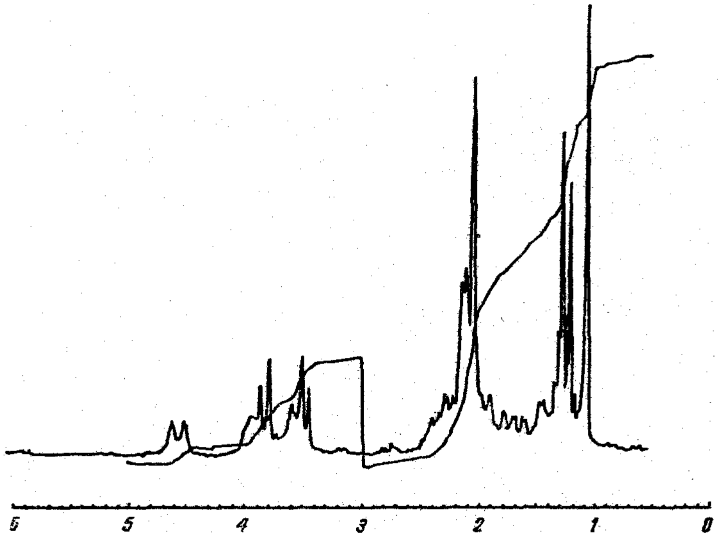


Fig. 2. NMR spectrum of alkhanol.

downfield by 0.1 ppm and is found at 1.16 ppm. Such a shift is characteristic for acetyl derivatives of sesquiterpene lactones in which the hydroxy group is present in the vicinal position to an angular methyl group (at C_1 or C_9) [2-4].

The composition, the presence of one double bond, the characteristics of the NMR spectrum, and also the absence of the signals of olefinic protons from this spectrum, indicate that alkhanol belongs to the group of sesquiterpene lactones based on a eudesmane or a pseudoguaiane carbon skeleton.

In view of the absence of the signals of olefinic protons from the spectrum, the — tetrasubstituted — double bond may be at C_4–C_5 or C_7–C_{11}. The tetrasubstituted position of the double bond is also shown by the signal of the lactone proton in the form of a doublet (at 4.57 ppm, J = 10 Hz).

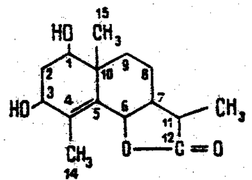
The double bond in alkhanol is difficult to reduce. Only hydrogenation in the presence of freshly-prepared PtO_2 (according to Adams) in a ratio of 1:5 led to a dihydro derivative with the composition $C_{15}H_{24}O_4$, mp 220-222°C, identified from its IR spectrum as dihydroerivanin (tetrahydroalkhanin).

Thus, the position of the hydroxy groups in the eudesmane carbon skeleton of the alkhanol molecule has been established. So far as concerns the position of the double bond in the compound under investigation, it is probably at C_4–C_5. The presence of the double bond in the lactone ring is unlikely, since, on the one hand this would cause an appreciable lowering of the frequency of the lactone carbonyl in the IR spectrum (by 15-20 cm^{-1}) so that the carbonyl band would be found in the 1740-1750 cm^{-1} region and, on the other hand, the absorption band in the 1650-1690 cm^{-1} region would be extremely strong [5], as in isoambrosin [6], isobadkhysidin [7], and the isomeric derivatives of peruvin [8], mexicanin A [9], flexuosin [10], and others [11]. However, the value of the band of the lactone carbonyl in the IR spectrum (1775, 1760 cm^{-1}) and the doublet of the secondary methyl group in the NMR spectrum (1.23 ppm), which is characteristic for a CH_3—CH< group adjacent to which there is a heteroatom, and also the low intensity of the band of the double bond, make it possible to suggest the C_4–C_5 position for the double bond.

The UV spectrum of alkhanol is also in harmony with the position of the double bond put forward above. As is well known [12], a tetrasubstituted double bond appears in the UV region of the spectrum at 196-200 nm. The UV spectrum of alkhanol has a maximum at 206 nm which is characteristic for a tetrasubstituted double bond occupying an exocyclic position with respect to ring B. It must be mentioned that when a double bond is present in the lactone ring, the UV spectrum usually shows a maximum in the 220-226 nm region.

To determine the position of the double bond, alkhanol was oxidized with chromium trioxide. Although this gave a mixture of substances, the UV spectrum showed the formation of a substance with a conjugated ketone group (maximum at 234 nm).

The production of tetrahydroalkhanin in the hydrogenation of alkhanol on the one hand, and the detection in the UV spectrum of the oxidized of a maximum at 234 nm, on the other hanc unambiguously show the position of the tetrasubstituted double bond in the molecule of the compound under investigation at C_4–C_5. Consequently, alkhanol has the structure (I).



I

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer in paraffin oil, the UV spectrum on a Specord UV-VIS spectrophotometer in ethanol, and the NMR spectra on a Varian HA-100D spectrometer in deuterochloroform with TMS as internal standard. The results of microanalysis corresponded to the calculated figures.

Isolation of Alkhanol. The dark green resin obtained from the epigeal part of *Artemisia fragrans* on extraction with acetone (15 g) was chromatographed on a colum (45×3.5 cm) containing neutral alumina (activity grade II), 100-ml fractions being collected. Elution was performed with hexane (15 fractions), mixtures of hexane and diethyl ether in ratios of 3:2 (eight fractions), 1:1 (three fractions), 1:2 (five fractions), 1:3 (seven fractions), and 1:4 (six fractions), and ether. Fractions 34-36, eluted by hexane—ether (1:3) yielded a crystalline substance with mp 179-181°C.

Acetylation of Alkhanol. A solution of 0.1 g of the substance in 3 ml of pyridine was treated with 3 ml of acetic anhydride. The mixture was heated on the water bath (10 min), left at room temperature for a day, and evaporated in a clock glass. This gave crystals with mp 194-196°C (from hexane—ether).

Hydrogenation of Alkhanol. A solution of 0.1 g of the substance in 20 ml of ethanol was hydrogenated in the presence of 0.5 g of freshly-prepared PtO_2 for 24 h, 10.5 ml of H_2 being consumed. The solution was filtered and the ethanol was distilled off. The residue was dissolved in a mixture of petroleum ether and diethyl ether and the solution was left at room temperature. The crystalline precipitate that deposited had, after four recrystallizations from the given mixture, mp 220-222°C. The initial lactone alkhanol was recovered from the first mother solution.

Oxidation of Alkhanol. A solution of 0.05 g of alkhanol in 1 ml of pyridine was treated with a solution of 0.02 g of chromium trioxide in 1.5 ml of a 95% solution of pyridine in water. The mixture was left overnight. Then 10 ml of 20% sulfuric acid was added and it was evaporated to half-volume and extracted with chloroform. The chloroform layer was washed with water, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue contained a mixture of substances.

SUMMARY

A new sesquiterpene lactone $C_{15}H_{22}O_4$ which has been called alkhanol has been isolated from the epigeal part of *Artemisia fragrans*.

It has been shown that alkhanol has the structure (I).

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^{13}C NMR SPECTRA OF HANDELIN AND ITS DERIVATIVES

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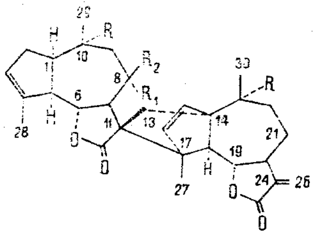
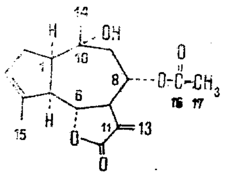
The ^{13}C spectra of the diguaiane lactone handelin (I), deacetylhandelin (II), handelin diacetate (III), and deacetyldehydrohandelin (IV), and also cumambrin A (V) — a known sesquiterpene lactone that is a component part of the molecule of the compound (I) and is isolated together with it from a single source — have been studied. The identification of the resonance lines was based on a comparison with one another of the ^{13}C NMR spectra of compounds (I-IV) and (V) obtained under conditions of complete and partial decoupling from protons, and an analysis of the chemical shifts of certain carbon atoms of the model lactone cumambrin A and their comparison with the analogous parameters of handelin and its derivatives. The α-, β-, and γ-contributions of the neighboring groups to the chemical shifts of the carbon atom considered, and, in individual cases, the contributions due to steric factors, were also taken into account. A complete assignment of the lines of the spectra has been made on the basis of the comparative consideration performed.

The new diguaianolide handelin was isolated from *Handelia trichophylla* Heimerl [1]. The main results of a study of the PMR spectra of handelin and its derivatives have been given in a previous paper [2].

In the present communication we discuss the results of a study of the ^{13}C NMR spectrum of handelin (I), deacetylhandelin (II), handelin diacetate (III), and deacetyldehydrohandelin (IV), and also of cumambrin A (V) — a known sesquiterpene lactone [3, 4] which is one of the component parts of the molecule of compound (I) and has been isolated together with the latter from a single source [5].



I. $R=OH; R_1=OAc; R_2=H$
II. $R=R_1=OH; R_2=H$
III. $R=R_1=OAC; R_2=H$
IV. $R=OH; R_1+R_2=O$



V

The resonance lines were identified by comparing with one another the ^{13}C NMR spectra of

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