STRUCTURE OF THE NEW GERMACRANOLIDE SHONACHALIN A FROM *Artemisia fragrans*

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The structure of a new germacranolide — shonachalin A isolated from *Artemesia fragrans* — has been established on the basis of chemical and spectroscopic (IR, UV, and ^1H and ^{13}C NMR) results.

By the chromatographic separation on a column of alumina (122 × 3 cm, Al_2O_3 of activity grade IV) of the total extractive substances obtained by the acetone extraction of the epigeal part of *Artemesia fragrans* Willd., collected in the village of Shonachala, Lerik region of the Azerbaidzhan SSR, we have isolated a substance belonging to the group of sesquiterpene lactones and have called it shonachalin A.

Shonachalin A (I) has the composition $C_{15}H_{22}O_4$. Its IR spectrum contained absorption bands of an OH group (3300-3500 cm^{-1}), of a γ-lactone ring (1770 cm^{-1}), and of double bonds (1670 and 1650 cm^{-1}). The acetylation of shonachalin A under the usual conditions [1] led to a monoacetyl derivative (II) with the composition $C_{17}H_{24}O_5$, mp 130-132°C (hexane—chloroform). The IR spectrum of the latter showed bands of an OH group (3320 cm^{-1}), of a lactone ring (1780 cm^{-1}), and of double bonds (1680 and 1650 cm^{-1}). The ^{13}C NMR spectrum of monoacetylshonachalin A with complete suppression of spin-spin coupling revealed 17 signals belonging to 17 carbon atoms with the sp^3 and sp^2 types of hybridization.

The off-resonance spectrum (here and below where the multiplicity of a signal is shown what is in view is the nature of the signal under conditions of incomplete decoupling from protons), showed the quartets of a secondary methyl group (15.77 ppm), of a vinyl methyl group (18.02 ppm), and of the methyl group of an ester (21.15 ppm). The presence of these methyl groups in the molecule was also confirmed by the ^1H NMR spectrum which contained doublets of $CH_3-CH<$ (1.33 ppm, J = 6.59 Hz), and $CH_3-\underset{|}{C}=$ (1.69 ppm, J = 1.22 Hz) groups and the singlet of a $CH_3-\underset{|}{C}=O$ (2.10 ppm) group.

The lactone under investigation contained two secondary hydroxy groups. This was shown, in the first place, by the presence in the off-resonance spectrum of the monoacetyl derivative of doublet signals at 74.99 and 76.62 ppm caused by the interaction of the gem-hydroxylic carbon and the gem-acetyl carbon with the corresponding geminal protons and, in the second place, by the presence in the ^1H NMR spectrum of the signals of protons of gem-hydroxy (at 3.85 ppm) and gem-acetyl (at 5.07 ppm) groups. Shonachalin A contained two double bonds. One of them, according to the off-resonance spectrum of the monoacetyl derivative, was that of an exomethylene group (t, 112.23, and s, 146.25 ppm), and the other was secondary-tertiary (q, 18.02; d 121.82; and s, 147.73 ppm). Because of superposition, the off-resonance spectrum of (II) did not permit the multiplicities of some of the signals to be determined. We therefore recorded the "Inept" ^{13}C NMR spectrum in which 13 signals belonging to three methyl, three cyclic methylene, five methine, one exocyclic methylene, and one olefinic (secondary-tertiary double bond) carbon atoms were found. Below we give details of the "Inept" ^{13}C NMR spectrum of monoacetylshonachalin (see following page).

Thus, according to the facts given above, shonachalin A is based on a germacrane carbon skeleton.

To determine the positions of the hydroxy groups and of the double bonds in the molecule of shonachalin A we oxidized it. This gave a hydroxy keto derivative (III) with the composition $C_{15}H_{20}O_4$, mp 145-147°C (hexane—chloroform). Its IR spectrum contained the band of an OH

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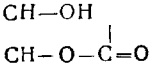
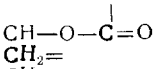
Carbon atom	Chemical shift, ppm	Grouping containing the carbon atom
13	15.77	CH_3 –
14	17.96	CH_3–
17	21.21	CH_3–
3	32.84	–CH_2–
2	36.27	–CH_2–
11	41.24	–CH–
9	42.42	–CH_2–
7	51.92	–CH–
1	74.96	–CH–OH
8	76.62	
6	78.24	
15	112.32	CH_2=
5	121.70	–CH=

group (3200-3370 cm^{-1}), of a γ-lactone ring (1770 cm^{-1}), of a conjugated ketone group (1670 cm^{-1}), and of a conjugated double bond (1625 cm^{-1}). The band of a second double bond (1670 cm^{-1}) present in the spectra of the initial lactone and its monoacetate was superposed on the band of the conjugated ketone group.

The UV spectrum of the oxidized product confirmed the presence of a conjugated ketone group (λ 241 nm, log ε 3.98).

The formation of a derivative with a conjugated ketone function showed the adjacency of one hydroxy group to a double bond. This idea was confirmed by the value of the chemical shift of the signal of the protons of the exomethylene groups (5.26 ppm) which appeared in the ^1H NMR spectrum of monoacetylshonachalin in the form of a broadened two-proton singlet shifted downfield by ~0.3 ppm. The paramagnetic shift of the signal of the exomethylene group was caused by the α position of a hydroxy group in relation to the methylenic double bond [1-3].

The signal of the gem-hydroxylic proton (H-1) in the spectrum of shonachalin A was found at 3.85 ppm. This signal had the form of an isosceles triangle with a half width $W_{1/2}$ = 16 Hz, which indicated the possibility of a triplet or quadruplet structure.

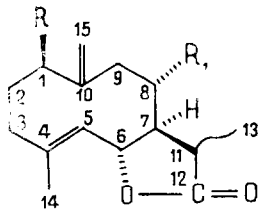
The second double bond – secondary-tertiary – was present at C_4–C_5, and the lactone ring at C_6–C_7. This was indicated by the following facts: In the first place, the signal of the lactone proton (H-6) in the ^1H NMR spectrum of (II) appeared in the form of a triplet at 4.45 ppm ($J_1 = J_2$ = 10 Hz). The ratio of the intensities of the components of the signal (1:2:1) showed interaction with only two vicinal protons. In the second place, the signal of the olefinic proton of the secondary-tertiary double bond had a doublet structure (at 5.20 ppm), likewise with a constant of 10 Hz. Each component of the doublet of the olefinic proton was additionally split by 1.22 Hz because of allyl interaction with the vinyl methyl group.

The second OH group in the shonachalin A molecule could be present at C-3, C-8, or C-9. However, the multiplicity of the structure of the signal of gem-acetyl proton (at 5.07 ppm) in the spectrum of (II) excluded the possibility that the OH group was present at C-3 or C-9; the half-width of this signal was 20 Hz. Consequently, the OH group was present at C-8 and had the α orientation. The presence of the OH group at C-8 was also confirmed by the ^{13}C NMR spectrum of monoacetylshonachalin A. Of the three cyclic methylene carbon atoms, the signal of one methyl group (C-9) resonanted in a weaker field (at 42.42 ppm) then the other signals of methylene groups. A similar paramagnetic shift of the signal of a cyclic methylene group has been observed in the ^{13}C NMR spectra of badkhysin, isobadkhysin [4], acetylartemisin [5], and handelin [6] and is due to the simultaneous Δ influence of a methylenic double bond and of an ester group. Furthermore, the C-7 signal (at 51.92 ppm) shifted somewhat downfield. The paramagnetic shift of the C-7 signal also caused by the β influence of the ester group.

The spin-spin coupling constants of H-1 (8 Hz), H-6 (10 Hz), H-7 (10 Hz), and H-8 (10 Hz) showed their α, β, α, and β-orientations, respectively. Thus, structure (I) is proposed for shonachalin A. (See following page.)

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in paraffin oil, UV spectra on a Specord UV-Vis spectrometer in ethanolic solution, and ^1H and ^{13}C NMR spectra on a Bruker WP 200SY spectrometer with a frequency for ^{13}C of 50.32 MHz in deuterated chloroform solutions with, as internal standard, TMS – 0.



I $R = R_1 = OH$

II $R = OH$; $R_1 = -O-\overset{O}{\overset{\|}{C}}-CH_3$

III $R = =O$; $R_1 = OH$

Isolation of Shonachalin A. The resin obtained by two acetone extractions (of four days each) of 634 g of the epigeal part of *Artemesia fragrans* (35 g, yield 5.52%) was chromatographed on a column of alumina (122 × 3 cm, Al_2O_3 of activity grade IV). The volume of each fraction was 100 ml. Elution was performed with hexane (12 fractions), hexane–ether (1:1) (50 fractions), ether (8 fractions), chloroform (15 fractions), and acetone (11 fractions), and fractions 88-89 were combined and rechromatographed on a column of alumina (45 × 15 cm, Al_2O_3 of activity grade IV). The volume of each fraction was 50 ml. Fractions were eluted with chloroform and with chloroform–acetone in ratios of 10:1, 8:2, 7:3, 6:4, 1:1, 1:2, and 1:3. The fractions eluted by chloroform–acetone (7:3) yielded a viscous oily substance with the composition $C_{15}H_{22}O_4$.

Acetylation of Shonachalin A. 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 left at room temperature for 24 h and was then evaporated on the water bath in a porcelain dish. The residue was dissolved in 5 ml of chloroform and chromatographed through a 15-cm layer of Al_2O_3 (d = 1.5 cm), with elution by 100 ml of chloroform. The solvent was distilled off and the residue was dissolved in a mixture of chloroform and hexane. On standing, a crystalline substance deposited with the composition of $C_{15}H_{24}O_5$, mp 130-132°C (hexane–chloroform).

Oxidation of Shonachalin A. A solution of 0.05 g of the substance in 3 ml of acetone was treated with a solution of 0.05 g of chromium anhydride in 3 ml of acetone. The mixture was left at room temperature and was then worked up in the usual way [7]. This gave a substance with the composition $C_{15}H_{20}O_4$, mp 145-146°C (hexane–chloroform).

SUMMARY

A new germacranolide — shonachalin A — has been isolated from *Artemisia fragrans* Willd. A structure has been proposed for it on the basis of chemical and spectral (IR, UV, and ^1H and ^{13}C NMR) characteristics.

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