Chemistry of Natural Compounds, Vol. 33, No. 6, 1997

STRUCTURE OF THE SESQUITERPENE LACTONE ARTAPSHININ

A. G. Safarova, S. V. Serkerov, and A. N. Aleskerova

UDC 582.4.581.19

On the basis of spectral characteristics (IR, ^1H and ^{13}C NMR spectroscopies) and chemical transformations it has been shown that the new sesquiterpene lactone artapshinin has the structure of 1β,3β-dihydroxy-6βH,7αH,11βH-germacra-4(5),10(15)-dien-6,12-olide.

The new sesquiterpene lactone artapshin isolated from *Artemis fragrans* Willd., gathered on Apsheron (Azerbaidzhan Republic), has been reported previously [1]. Not one of the sesquiterpene lactones (alchanene, alkhanin, alkhanol, erivanin) characteristic for *Artemisia fragrans* was detected in this plant material.

Continuing the study of the sesquiterpene lactones of this plant material we have isolated a substance with the composition $C_{15}H_{22}O_4$ (**1**), the IR spectrum of which had the absorption band of OH groups (3430 cm^{-1}) of the CO of a γ-lactone ring (1765 cm^{-1}), and of double bonds (1670, 1640 cm^{-1}). On acetylation, (**1**) formed a diacetate. The IR spectrum of the diacetate had the bands of a lactone CO (1790 cm^{-1}), of the CO groups of acetyl residues (1735, 1260, 1240 cm^{-1}), and of double bonds (1670, 1650 cm^{-1}). There was no band of hydroxy groups.

After having compared the physicochemical properties of the lactone under investigation and its diacetyl derivative, we came to the conclusion that it was new, and for it we have proposed the name artapshinin.

In the ^1H NMR spectrum of diacetylartapshinin (**2**) a doublet appeared at 1.18 ppm (J = 7 Hz, 3H, CH_3—CH< at C11), a broadened singlet at 1.76 ppm (3H, $CH_3-C=$), and singlets at 1.90 and 2.01 ppm (3H each, $CH_3-\overset{|}{C}=O$). A one-proton broadened singlet at 5.27 ppm and a doublet at 5.36 ppm (J = 2 Hz) showed the presence of an exomethylene group in the molecule of the substance. The signal of a lactone proton was found in the spectrum in the form of a triplet at 4.65 ppm (1H, $J_1 = J_2 = 10$ Hz) with a ratio of the intensities of the components of 1:2:1.

In view of the presence in the ^1H NMR spectrum of signals corresponding to $CH_3-CH<$, $CH_3-C=$, and $CH_2=C-$ groups, it could be assumed that the compound was based on a germacrane or guaiane carbon skeleton. The choice was made on the basis of the ^{13}C NMR spectrum of the diacetate taken with incomplete suppression of spin–spin coupling (off-resonance).

The spectrum contained 19 signals (Table 1), including 4 quartets (CH_3 groups), 4 triplets (CH_2 groups), 6 doublets (CH groups) and 5 singlets ($-\overset{|}{C}-$, $-\overset{|}{C}=$ and $-\overset{|}{C}=O$). As can be seen from the figures given in Table 1, one triplet (at 112.90 ppm, $J_{CH} = 157.21$ Hz) was observed in the spectrum in the region of sp^2-hybridized carbon atoms and belonged to the carbon of an exomethylene group. The other triplets, appearing in the region of sp^3-hybridized carbon atoms, characterized three ring methylene groups.

Thus, with the presence of two double bonds and three cyclic methylene groups, the compound under investigation could only be based on a germacrane carbon skeleton.

As we have noted, artapshinin contains two double bonds. One of them is a methylene bond, the second is secondary–tertiary (s, 1.66; 3H and d, 5.3 ppm, J = 10 Hz, 1H). The doublet structure of the signal of the olefinic proton and the spin–spin coupling constant (SSCC) permitted us to ascribe the C4–C5 position to the secondary–tertiary bond. This point of view was confirmed by the signal of the lactone proton, which had a triplet structure with the SSCC 10 Hz.

To determine the positions of the hydroxy groups in the molecule, we used the ^1H NMR spectrum of diacetylartapshinin. In the weak-field region of the spectrum there were two one-proton quartets relating to two gem-acetyl

Institute of Botany, Academy of Sciences of the Azerbaidzhan Republic, Baku. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 837-840, November-December, 1997. Original article submitted April 8, 1996.

00093130/97/3306-0655$18.00

TABLE 1

Carbon atom	Multiplicity*	Chemical shift, ppm	J_{CH}, Hz
1	d	71.17	147.96
2	t	43.76	129.47
3	d	75.85	146.11
4	s	146.67	–
5	d	121.09	157.21
6	d	78.68	140.57
7	d	53.36	133.17
8	t	31.23	129.47
9	t	36.71	125.77
10	s	143.78	–
11	d	38.54	147.97
12	s	178.13	–
13	q	9.66	129.47
14	q	17.48	125.77
15	t	112.90	157.21
16	s	169.86	–
17	q	20.94	129.47
18	s	169.64	–
19	q	20.79	129.47

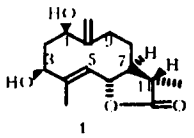
*d) Doublet; t) triplet; q) quartet; s) singlet.

protons (the ratio of the intensities of the components of each quartet was 1:1:1:1). A quartet at 4.75 ppm (J_1 = 10, J_2 = 5 Hz) was analogous to the signal of the gem-acetyl proton of artapshinin [1], which made it possible to assume the position of one hydroxy group at C1 and its β- orientation.

A quartet at 4.86 ppm (J_1 = 10, J_2 = 2 Hz, 1H), belonging to the other gem-acetyl proton showed interaction of this proton with only two vicinal protons. Therefore, the second hydroxy group in the molecule of the substance could be located at C3 or C9. However, in favor of the C3 position was the chemical shift (CS) of the cyclic methylene groups in the ^{13}C NMR spectrum. In the spectrum, the signal of the carbon of one of the methylene groups, C2, was present in a relatively weak field (at 43.76 ppm) as compared with the signals of the other $-CH_2$ groups. In the ^{13}C NMR spectrum of alkhanin [7], in which the positions of the functional groups and of the endocyclic double bond are analogous to those of the compound under investigation, the signal of the C2 methylene carbon is found at 43.30 ppm, and the CSs of the carbons of the other methylene groups of the compounds compared are, in the main, close to one another. The small differences that do exist are possibly due to the weak-field influence of the methylenic double bond and the acetyl groups on the CSs of C8 and C9.

Thus, on the basis of the facts given above, artapshinin corresponds to the structure of 11,13-dihydroridentin [8].

With the aim of obtaining chemical confirmation, artapshinin was oxidized with chromic anhydride and was then dehydrated with 50% sulfuric acid [9]. It must be mentioned that the dehydration conditions used in [9] coincide with the cyclization conditions used in [10]. Consequently, the formation of a compound with a eudesmane or guaiane carbon skeleton was possible. From the reaction mixture we isolated a substance with the composition $C_{15}H_{18}O_3$, mp 137-138°C, the IR spectrum of which contained the bands of the CO group of a γ-lactone ring (1780 cm^{-1}), of a cyclohexenone system (1670 cm^{-1}), and of conjugated double bonds (1630 and 1585 cm^{-1}). By a direct comparison of IR spectra, the substance was identified as anhydrotauremisin [9]. We have also obtained anhydrotauremisin by the chromic anhydride oxidation of erivanin [11].



1

EXPERIMENTAL

The IR spectra of the crystalline substances were taken in paraffin oil on a UR-20 spectrophotometer, and ^1H and ^{13}C NMR spectra on a Bruker WP 200 SY 50.30 MHz spectrometer in $CDCl_3$. Internal standard: TMS — 0. CSs are given on the δ-scale.

Isolation of Artapshinin. The extraction of the plant material and column chromatography were performed as in the isolation of artapshin [1]. The fractions eluted by chloroform yielded a viscous substance with the composition $C_{15}H_{22}O_4$.

Acetylation of Artapshinin. A solution of 0.1 g of (**1**) in 3 ml of pyridine was treated with 3 ml of acetic anhydride, and the reaction mixture was kept at room temperature for 24 h and was worked up by a known method. This gave a substance with the composition $C_{19}H_{26}O_6$, mp 177-178°C (from aqueous methanol).

Preparation of a Ketodiene Lactone. A solution of 0.2 g of artapshinin in 5 ml of acetic acid was treated with a solution of 0.2 g of CrO_3 in 5 ml of acetic acid. The reaction mixture was stirred, left at room temperature for 2 h, and worked up in the usual way [8]. The residue was dissolved in 5 ml of ethanol, and 10 ml of 50% sulfuric acid was added. The resulting solution was heated on the water bath for 20 min, and it was then cooled, diluted with water, and extracted with chloroform. The chloroform extracts were washed with water to neutrality, dried, filtered, and evaporated. The residue consisted of a mixture of substances the chromatographic separation of which gave 60 mg of one with the composition $C_{15}H_{18}O_3$, mp 137-138°C.

REFERENCES

1. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 578 (1983).
2. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 632 (1990).
3. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 75 (1978).
4. S. V. Serkerov and A. N. Aleskerova, Khim. Prir. Soedin., 488 (1979).
5. A. D. Kagarlitskii, S. M. Adekenov, and A. N. Kupriyanov, Sesquiterpene Lactones of the Plants of Central Kazakhstan [in Russian], Nauka, Alma-Ata (1987).
6. R. G. Kelsey and F. Shafizadeh, Phytochemistry, **18**, 1591 (1979).
7. S. V. Serkerov, Khim. Prir. Soedin., 455 (1982).
8. M. A. Irvin, K. H. Lee, R. F. Simpson, et al., Phytochemistry, **8**, 2009 (1969).
9. K. S. Rybalko, A. I. Ban'kovskii, and V. I. Sheichenko, Natural Sesquiterpene Lactones, Medicinal Plants [in Russian], Moscow, Vol. 15 (1969) p. 168.
10. I. S. Akhmedov, Sh. Z. Kasymov, and G. P. Sidyakin, Khim. Prir. Soedin., 691 (1970).
11. S. V. Serkerov, Terpenoid and Phenolic Compounds of Plants of the Families *Asteraceae* and *Apiaceae* [in Russian], Doctoral Dissertation in the form of a lecture, Tashkent (1991).