A NEW COMPONENT OF *Artemesia hanseniana*

S. V. Serkerov and A. N. Aleskerova

UDC 547.913

A sesquiterpene lactone with mp 97-99°C, $C_{15}H_{20}O_3$, identified as deoxy-ψ-santonin, has been isolated from the epigeal part of *Artemisia hanseniana* var. *phylostachus*.

The isolation and identification of sesquiterpene lactones from the epigeal part of *Artemisia hanseniana* var. *phylostachus* has been reported previously [1]. The present paper gives the results of a study of a stereoisomer of taurin — a new component of this species of wormwood.

Substance (I) has the composition $C_{15}H_{20}O_3$, mp 97-99°C (from methanol), $[\alpha]_D - 198.7°$ (c 0.87; ethanol). According to its composition, the molecule has three oxygen atoms. Two of them form part of a γ-lactone ring (1775 cm^{-1}), and the third is in a ketone group (1715 cm^{-1}). The assignment of the band at 1715 cm^{-1} in the IR spectrum to a ketone group was made on the basis of the fact that when the substance was reduced with sodium tetrahydroborate in methanol a new band appeared at 3440 cm^{-1} (OH group) in place of the maximum at 1715 cm^{-1}.

The compound under consideration is based on a bicyclic carbon skeleton: eudesmane or pseudoguaniane. This is shown by the detection in its NMR spectrum of a singlet signal (at 1.28 ppm) due to an angular methyl group $\left(CH_3-\overset{|}{\underset{|}{C}}-\right)$. The elementary composition of the bicyclic carbon skeleton, and the presence in the NMR spectrum of only one doublet of a secondary methyl group shows that the molecule of the substance contains a double bond. There are no signals of olefinic protons in the NMR spectrum. The singlet of a vinylmethyl group (at 1.96 ppm, $CH_3-\underset{|}{C}=$) characterizes the double bond as tetrasubstituted, and therefore the double bond can be present only at C_4—C_5 or C_7—C_{11}. The latter position is exluded by the UV and IR spectra. The presence of a double bond in the lactone ring (at C_7—C_{11}) would cause, on the one hand, a considerable lowering of the frequency of the lactone carbonyl in the IR spectrum and, on the other hand, the appearance of a maximum in the 220-226 nm region of the UV spectrum [2].

The carbon skeleton of compound (I) was determined by the hydrogenation method. The dehydrogenation of the substance previously reduced with sodium tetrahydroborate over selenium at 280-240°C for 40 h led to 7-ethyl-1-methylnaphthalene, which was identified through its picrate with mp 94-95°C. These results indicate that, like taurin [3], tauremisin [4], and badkhyzin [5], the substance belongs to the group of sesquiterpene lactones based on the eudesmane (selinane) carbon skeleton.

The ketone group is probably located at C-1. This is deduced, in the first place, from the point of view of biogenesis, since in the molecule of each one of the sesquiterpene lactones isolated from *Artemisia hanseniana* (artemin, erivanin, tauremisin, and taurin) one of the functional groups (OH or CO group) is present at C-1, and, in the second place, from the value of the chemical shift of the angular methyl group of 1.28 ppm, which is characteristic for methyl groups in the α position to which there is a ketone group [3, 4].

Thus, the substance has a structure similar to that of the known lactone taurin [3]. It differs from the latter stereochemically. In actual fact, in a comparison of the IR spectra of compound (I) and taurin, a difference is observed in the "fingerprint" region characteristic of isomeric compounds.

It must be mentioned that the spatial orientation of the substituents has not been given for taurin [3, 6]. The lactone proton of taurin (H-6) appears in the form of a doublet

---

V. L. Komarov Institute of Botany of the Academy of Sciences of the Azerbaidzhanian SSR, Baku. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 564-568, September-October, 1981. Original article submitted June 18, 1981.

0009-3130/81/1705-0404$07.50

TABLE 1

Compound	Chemical shift, ppm			
	$CH_3-\overset{\vert}{\underset{\vert}{C}}-$	$CH_3-CH<$	$CH_3-\underset{\vert}{C}$	lactone proton
Substance (I), in $CdCl_3$	s 1.28	d 1,40	s 1,96	d 5,47 J = 5 Hz
The same in C_6D_6	s 1,16	d 1,03	s 1.61	d 5.12 J = 5 Hz
$\Delta\delta = \delta_{CDCl_3} - \delta_{C_6D_6}$	0,12	0,37	0.35	0,35
Taurin in $CdCl_3$	s 1.33	d 1,22	s 1,96	d 4,56 J = 11 Hz
The same in C_6D_6	s 1,08	d 1,00	s 1.84	d 4.12 J = 11 Hz
$\Delta\delta = \delta_{CDCl_3} - \delta_{C_6D_6}$	0.25	0,22	0,12	0,44

Note. s — singlet; d — doublet.

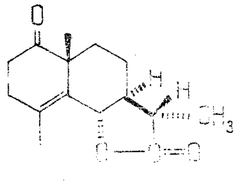
with its center at 4.56 ppm and a spin—spin coupling constant (SSCC) of 11 Hz. This means that H-6 and H-7 are trans with respect to one another. The signal of the lactone proton of the compound under investigation likewise appears in the form of a doublet at 5.47 ppm (J = 5 Hz). As we see, the signal of the lactone proton of taurin is shifted upfield by 0.91 ppm in comparison with the signal of the analogous proton of compound (I). Such a shift is characteristic for stereoisomers with respect to the methyl group at C-11 (α and β) [7, 8]. Consequently, the methyl group at C-11 in the molecule of substance (I) has the β orientation, and in taurin the α orientation, similarly to α- and β-santonins [7], and artemin and arsubin [8]. The correctness of this point of view is also shown by the value of the upfield shift of the signal of the CH_3-C_{11} group of the compounds being compared in the NMR spectra taken in C_6D_6 as compared with those in $CDCl_3$ [9, 10] (Table 1).

The SSCC (5 Hz) of the lactone proton of the compound under investigation permits the cis orientation to be assigned to the lactone ring.

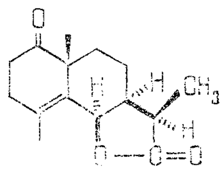
It must be mentioned that a paramagnetic shift by 0.91 ppm of the H-6 signal of compound (I) as compared with the H-6 doublet of taurin is somewhat greater than the observed shift in lactones with the α and β orientations of the methyl group at C-11.

For example, the H-6 signal in the NMR spectrum of β-santonin is shifted downfield by 0.21 ppm as compared with the signal of α-santonin [7], and in the spectrum of acetylarsubin the paramagnetic shift of the same signal is 0.23 ppm as compared with the signal of artemin [8]. The paramagnetic shift of the H-6 doublet for compound (I) is also caused by the cis orientation of the lactone ring. For example, on passing from badkhyzin to isobadkhyzin the signal of the lactone proton shifts downfield by 0.30 ppm [11], although the CH_3-C_{11} groups in them have the same (β) orientation [12].

Thus, compound (I) has the structure and configuration of 1-oxo-6α, 7α, 11αH-eudesm-4-en-6,12-olide (I) and taurin the configuration 1-oxo-6β, 7α, 11βH-eudesm-4-en-6,12-olide (II).



II



I

Sesquiterpene lactones differing from taurin stereochemically have been reported in the literature [13-15].

Finitin, $C_{15}H_{20}O_3$, mp 153-155°C, $[\alpha]_D^{12} - 167.7°$ ($CHCl_3$; c 1.7). This has the structure of 1-keto-6α, 7α, 11β H-eudesm-4-en-6,12-olide, differing from taurin by the stereochemistry of the C-6 asymmetric center and from compound (I) by that at the C-11 center.

TABLE 2

Compound	NMR spectrum, ppm Hz					IR spectrum, cm^{-1}
	$CH_3-\overset{\vert}{\underset{\vert}{C}}-$	CH_3-CH	$CH_3-\underset{\vert}{C}=$	lactone CH	CH at the OH group	
Artesin	c 1,02	d 1,14 J=10	s 1,75	d 4,45 J=9	t 3,47 J=10	3490,1750 1660
Dihydrotaurin	c 1,02	d 1,15 J=8	s 1,75 J=1,5	d 4,50 J=9	t 3,45 J=10	3500,1758 1668

Deoxy-ψ-santonin, $C_{15}H_{20}C_3$, mp 101.3-101.9°C, $[\alpha]_D - 207°$ (ethanol, c 0.68) has the structure of 1-oxo-6α, 7α, 11αH-eudesm-4-en-6,12-olide, and it differs from taurin by the stereochemistries of the C-6 and C-11 asymmetric centers [just like compound (I)]. Consequently, the structures and configurations of compound (I) and of deoxy-ψ-santonin are similar, i.e., they are identical. This is the first time that deoxy-ψ-santonin has been isolated from *A. hanseniana*.

Recently [16], two sesquiterpene lactones have been isolated from *Artemisia granetensis* Boiss. and their structures have been determined: $C_{15}H_{20}O_3$, mp 109-110°C, $[\alpha]_D - 109°$ (ethanol, c 0.2), 1-oxo-6β, 7α, 11βH-eudesm-4-en-6,12-olide (III), and $C_{15}H_{22}O_3$, mp 177-178°C, $[\alpha]_D + 60.9°$ (c 0.23), 1-hydroxy-6β, 7α, 11βH-eudesm-4-en-6,12-olide (IV). The melting points and $[\alpha]_D$ values of compound (III) are close to those of taurin. The structures and configurations of the lactones compared are identical.

In its physicochemical properties (composition, melting point, $[\alpha]_D$ etc.), 1-hydroxy-6β, 7α, 11βH-eudesm-4-en-6,12-olide resembles the sesquiterpene lactone artesin (V) [17]. In its turn, according to the results of Akyev et al. [17], the spectral characteristics and melting point of artesin are similar to those of dihydrotaurin. The identity of these compounds is shown by the following facts: The oxidation of (IV) leads [16] to 1-oxo-6β, 7α, 11βH-eudesm-4-en-6,12-olide, which we have identified as taurin. Artesin also forms taurin on oxidation [17]. Consequently, the stereochemistry of the C-6, C-7, and C-11 asymmetric centers in these compounds is the same. Hence, they can differ from one another only by the orientation of the OH group. As is known [17] the OH group in artesin has the β orientation. The hydrogenation of (IV) gives dihydrobalchanin [16, 18], the OH group in which also has the β orientation.

So far as concerns the stereochemistry of the OH group of dihydrotaurin, it must be mentioned that the signal of the hemihydroxylic proton in the NMR spectrum of the latter appears in the form of a triplet with an SSCC of 10 Hz, showing the β orientation of the hydroxy group. The IR and NMR spectra of artesin coincide with those of dihydrotaurin (Table 2).

Thus, artesin, 1-hydroxy-6β, 7α, 11βH-eudesm-4-en-6,12-olide and dihydrotaurin are identical.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer in paraffin oil, UV spectra on a Specord UV-Vis spectrometer, and NMR spectra on a Varian HA-100D instrument.

Isolation of Compound (I). Fraction 2, obtained by a method described previously [1] was rechromatographed in a column of alumina (activity grade (II) 30 × 1.5 cm). Elution was performed with hexane—ether (4 : 1). The volume of each fraction was 100 ml. A crystalline substance was obtained from fraction 2 which, after recrystallization from aqueous methanol, had mp 97-99°C.

Reduction of Compound (I) with $NaBH_4$. A mixture of 0.15 g of the substance in 3 ml of methanol and 0.5 g of $NaBH_4$ in 10 ml of methanol was kept for 2 h (until the reaction ceased), diluted with water, acidified with 10% H_2SO_4, and extracted with chloroform, and the extract was washed with water. Then it was dried over Ha_2SO_4, filtered, and evaporated. The residue consisted of a viscous oil.

Dehydrogenation. A mixture of 0.15 g of the reduced product of compound (I) and 0.15 g of selenium was heated at 280-340°C for 40 h. From the reaction mixture petroleum ether eluted a liquid hydrocarbon which was purified by passage through a small layer of alumina. Then it was treated with a hot ethanolic solution of picric acid. Crystals deposited in the form of orange needles with mp 94-95°C (7-ethyl-1-methylnaphthalene picrate).

SUMMARY

1. From the epigeal part of *Artemisia hanseniana* var. *phylostachus* a sesquiterpene lactone has been isolated with the composition $C_{15}H_{20}O_3$, mp 97-99°C, and it has been identified as deoxy-ψ-santonin.

2. The stereochemistry of taurin has been established.

3. The identity of the sesquiterpene lacton 1-oxo-6β, 7α, 11βH-eudesm-4-en-6,12-olide isolated from *Artemesia granatensis* Boiss. with taurin has been shown.

4. It has been established that the sesquiterpene lactones artesin, 1-hydroxy-6β, 7α, 11βH-eudesm-4-en-6,12-olide, and dihydrotaurin are identical.

LITERATURE CITED

1. S. V. Serkerov, R. M. Abbasov, and A. M. Aleskerova, Khim. Prirodn. Soedin., 665 (1976).
2. S. V. Serkerov, Khim. Prirodn. Soedin., 326 (1979).
3. N. A. Kechatova, K. S. Rybalko, V. I. Sheichenko, and L. P. Tolstykh, Khim. Prirodn. Soedin., 205 (1968).
4. K. S. Rybalko and L. Dolejs, Collect. Czech. Chem. Commun., 26, 2909 (1961).
5. S. V. Serkerov, Khim. Prirodn. Soedin., 590 (1971).
6. K. S. Rybalko, Natural Sesquiterpene Lactones [in Russian], Moscow (1978), p. 239.
7. High Resolution NMR Spectra, Japan Electron Optics Lab. Co. Ltd.,
8. V. A. Tarasov, Sh. Z. Kasymov, and G. P. Sidyakin, Khim. Prirodn. Soedin., 676 (1973).
9. C. R. Narayanan and N. K. Venkatasubramaniam, J. Org. Chem., 33, 3156 (1968).
10. W. Herz. P. S. Subramaniam, and T. A. Geissman, J. Org. Chem., 33, 3743 (1968).
11. S. V. Serkerov and V. I. Sheichenko, Khim. Prirodn. Soedin., 425 (1970).
12. S. V. Serkerov, Khim. Prirodn. Soedin., 629 (1980).
13. T. Kawawani and T. Takeuchi, J. Pharmac. Soc. Jpn. 74, No. 7, 793 (1954).
14. W. G. Dauben, J. S. P. Schwarz, W.K. Hayes, and P. D. Paul, J. Am. Chem. Soc., 82, 2239 (1960).
15. R. G. Kelsey and F. Shafizadeh, Phytochemistry, 18, 1591 (1979).
16. A. G. Gonzalez, J. L. Breton, and J. Stockel, An. Quim., 70, 231 (1974).
17. B. Akyev, Sh. Z. Kasymov, and G. P. Sidyakin, Khim. Prirodn. Soedin., 733 (1972).
18. S. P. Pathak, B. V. Bapat, and G. H. Kulkarni, Chem. Ind. (London), No. 35, 1147 (1970).