A NEW SESQUITERPENE γ-LACTONE, SIEVERSININ

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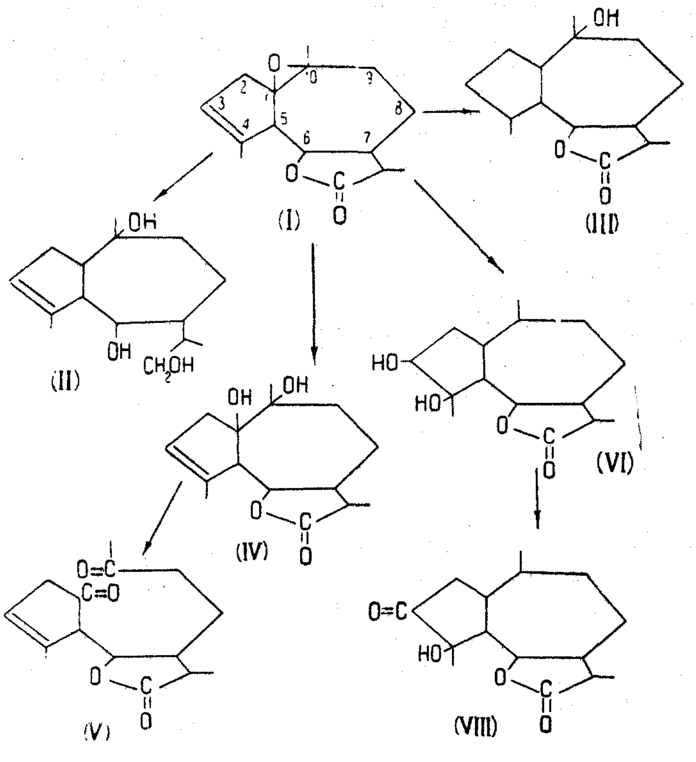
From the essential oil of Artemisia sieversiana Willd. and also from the green mass of the plant, we have isolated by extraction with petroleum ether a substance $C_{15}H_{20}O_3$ with mp 141°–142° C, $[\alpha]_D^{20}$ +57° which is a γ-lactone (1770 cm^{-1}). It contains one double bond (dibromide with mp 126° C) and an oxide ring. We have called it sieversinin.

The IR spectrum of this substance is similar to that of arborescin $C_{15}H_{20}O_3$ with mp 45° C, $[\alpha]_D^{20}$ +60° (Fig. 1). The NMR spectra of the two substances practically coincide (Fig. 2). On the basis of these results, sieversinin has been assigned the carbon skeleton of a guaian-6, 12-olide (I).

The reduction of sieversinin with lithium aluminum hydride led to a triol (II) with mp 162° C. On hydrogenation under various conditions, the substance under investigation absorbed 2 moles of hydrogen, forming, like artabsin [3, 4] and arborescin [2], a mixture of stereoisomers (III) containing a hydroxy group as a result of the opening of the oxide ring. From the mixture of products obtained by the hydrogenation of the substance in alcohol in the presence of platinum we isolated a crystalline isomer with mp 129.5° C, while on hydrogenation in ethyl acetate in the presence of palladium we isolated two isomers: a crystalline compound with mp 126° C and a liquid. The IR spectra of the substances isolated (Fig. 3) are similar to the IR spectra of the stereoisomeric products of the hydrogenation of artabsin, tetrahydroartabsin b with mp 158°–159° C and tetrahydroartabsin c with mp 136° C. This enables us to assume that one end of the oxygen bridge in sieversinin is located at C_{10}.



The hydration of sieversinin with 20% sulfuric acid in acetic acid formed a diol (IV) with mp 202° C, which was oxidized by periodic acid. Consequently, the diol is an α-glycol, and the substance contains an α-oxide ring. The product of the oxidation of the glycol with periodic acid (V) gave a positive iodoform reaction, which agrees with our assumption of the position of one end of the oxygen bridge on a carbon atom attached to a CH_3 group. The position of the second end of the bridge at C_1 follows from the IR spectrum of substance (V), since it contains a frequency characteristic for the CO group of a five-membered ring (1724 cm^{-1}).

We showed the presence of one double bond in sieversinin by preparing its dibromide with mp 126° C, $C_{15}H_{20}O_3Br_2$. The oxidation of sieversinin at the double bond with osmic acid led to a diol (VI) with mp 161°–162° C. The product of its oxidation with periodic acid (VII) gave a positive iodoform reaction. This shows that one end of the double bond in sieversinin is located on a carbon atom attached to a CH_3 group. The diol (VI) was oxidized with chromic anhydride. The product (VIII) contains a CO group in a five-membered ring. Thus, the double bond in sieversinin is at C_3.

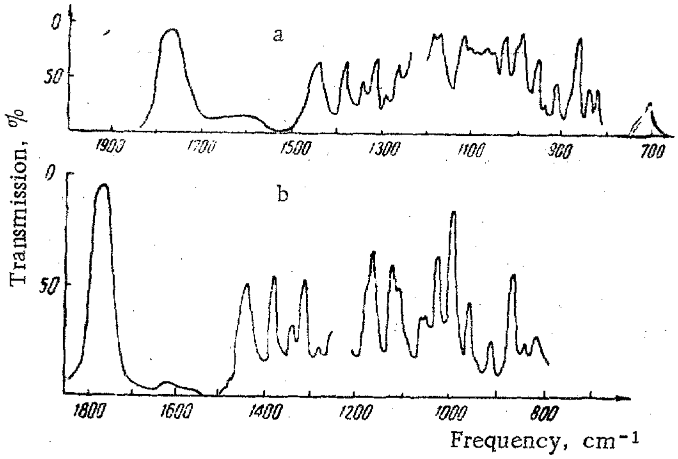


Fig. 1. IR spectra: a) Arborescin [1]; b) sieversinin.

The results of the chemical investigation agree with those of the NMR spectrum of the substance. We interpret this spectrum in a manner similar to that used for arborescin [2]. According to the spectrum, sieversinin contains a vinyl proton (signal at 4.05 τ) and a vinyl CH_3 group (signal at 8.09 τ). Consequently, the double bond of the substance must be located either at C_3 or at C_9. But since the proton at C_6 (signal at 6.05 τ) strongly interacts with an allyl proton (signal at 7.11 τ), the double bond must be at C_3. The spectrum has no other signals between 4.05 and 7.11 τ apart from the signal of a proton at C_6. Consequently, the oxygen bridge in the substance is attached to tertiary carbon atoms, i.e. to C_1 and C_{10}. This is confirmed by the fact that the spectrum has a signal at 8.65 τ which relates to a CH_3 group attached to an oxide ring. Thus, we have come to the conclusion that sieversinin possesses structure (I), which has recently been shown for arborescin [2, 4]. However, it is not identical with the guaienolide arborescin.

On dehydrogenation with sulfur, arborescin gives chamazulene in high yield [3, 5]. Under the same conditions, sieversinin formed scarcely detectable traces of chamazulene. The melting point of the hydration product of sieversinin (IV) is 202° C, and that of the analogous derivative of arborescin is 175° C. The hydrogenation of arborescin in ethyl acetate (Pd) gave a product with mp 136° C [3, 6]. On hydrogenating sieversinin under the same conditions, we obtained a substance with mp 126° C.

The IR spectra of arborescin and sieversinin, and also the products of their hydrogenation, have some differences, in spite of their similarity (cf. Fig. 3), while the IR spectra of the products of the hydrogenation of arborescin are identical with the IR spectra of tetrahydroartabsins b and c [2], and the IR spectra of the products of the hydrogenation of sieversinin do not coincide completely with either of them.

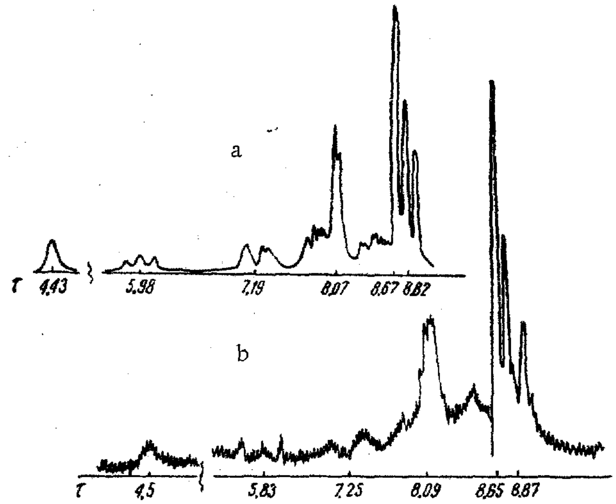


Fig. 2. NMR spectra: a) Arborescin [2], 60 Hz, $CDCl_3$; b) sieversinin, 40 Hz, $CHCl_3$.

Suchý, Herout, and Šorm [4] have previously reported a hydrogenation product of artabsin, tetrahydroartabsin d with mp 128° C, which has an IR spectrum differing in the details of the fine spectra from the IR spectra of tetrahydroartabsin c. Unfortunately, the authors mentioned do not give the IR spectrum of substance d and we were unable to compare it with the IR spectra of the products of the hydrogenation of sieversinin.

Taking the information given into account, it may be stated that the substance that we have isolated is a stereoisomer of arborescin.

Experimental

Isolation of sieversinin. 1. A petroleum ether solution of the essential oil of Artemisia sieversiana was filtered through a funnel containing alumina (activity grade II). The oxygen compounds absorbed by the alumina were extracted with ether. After standing, the concentrated ethereal solution deposited a substance with mp 142° C (alcohol), $[\alpha]_D^{20}$ +57° (chloroform).

Found, %: C 72.49; H 8.26. Calculated for $C_{15}H_{20}O_3$, %: C 72.55; H 8.12.

We obtained a crystalline dibromide of this substance with mp 123°–124° C; after recrystallization from alcohol it had mp 126° C.

Found, %: C 44.25; H 4.94. Calculated for $C_{15}H_{20}O_3Br_2$, %: C 44.11; H 4.84.

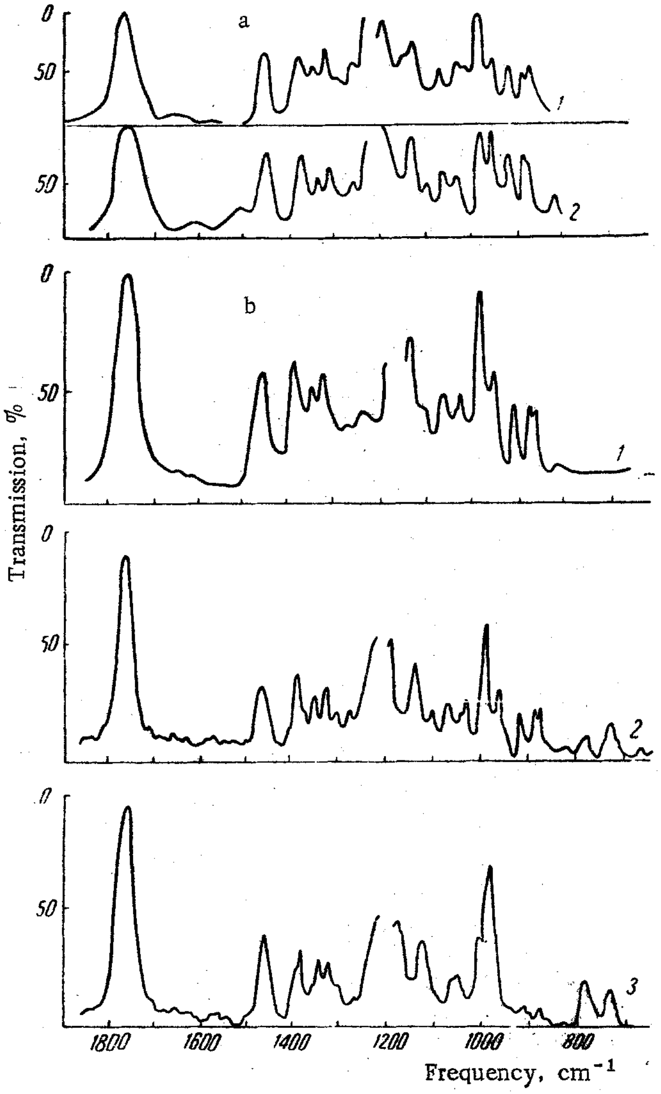


Fig. 3. IR spectra of the products of the hydrogenation of artabsin (a): 1) substance b; 2) substance c; and of sieversinin (b): 1) substance with mp 129.5° C; 2) substance with mp 126° C; 3) liquid product.

2. The epigeal part of Artemisia sieversiana was extracted with petroleum ether. When the concentrated extract was allowed to stand, a substance identical with that described above crystallized out.

The reduction of sieversinin with $LiAlH_4$. With stirring, a solution of 0.584 g of sieversinin in 20 ml of ether was gradually added to a solution of 0.315 g of $LiAlH_4$ in 45 ml of the same solvent. The mixture was heated in a water bath for 1 hr. Then, to decompose the excess of $LiAlH_4$, it was treated with 1.5 ml of alcohol and 50 ml of 10% sulfuric acid. Water was added and the triol formed was extracted with ether. This gave 0.40 g of colorless acicular crystals which, after recrystallization from alcohol and drying over phosphorus pentoxide, melted at 162° C.

Found, %: C 70.56; H 9.62. Calculated for $C_{15}H_{26}O_3$, %: C 70.59; H 10.02.

Hydrogenation of sieversinin. 1. 1 g of sieversinin was hydrogenated over 0.5 g of Adams' platinum catalyst in alcohol until saturation was complete, 204 ml of hydrogen being absorbed. The reaction product was a friable hygroscopic mass. When ether was added to it, a crystalline substance with mp 129.5° C (ether) deposited. The IR spectrum of the substance contained the frequency of an OH group.

Found, %: C 71.47; H 9.63. Calculated for $C_{15}H_{24}O_3$, %: C 71.39; H 9.59.

2. 0.5 g of sieversinin was hydrogenated over palladium (0.2 g) in ethyl acetate until saturation was complete. After the solvent had been distilled off, 0.5 g of a glassy mass was obtained. When it was chromatographed on alumina (activity grade IV), benzene extracted a liquid substance, and benzene–ether (1:1) a crystalline substance with mp 126° C. The substances each gave one spot, shown up by treatment with iodine vapors, on thin-layer chromatography [Al_2O_3, activity grade III, petroleum ether–ether (1:1)], the spots having different R_f values. The IR spectra of the substances contained the frequency of an OH group.

Hydration of sieversinin. A solution of 0.5 g of the substance in 7.5 ml of acetic acid was cooled to 0° C, and 1.5 ml of 20% sulfuric acid was gradually added. After 10 min standing, the reaction mixture was diluted with water and the hydration products were extracted with ether. The extracts were dried over sodium sulfate and the ether was distilled off. The residue, 0.37 g of a brown mass, was transferred to a column of alumina (2.2 g, activity grade III).

Elution with petroleum ether gave the starting material. Benzene extracted a diol with mp 198° C; after recrystallization from alcohol mp 202° C, $[\alpha]_D^{20}$ +148° C (c 0.676; chloroform). Weight 0.15 g.

Found, %: C 67.33; H 8.41. Calculated for $C_{15}H_{22}O_4$, %: C 67.66; H 8.38.

Oxidation of the diol with mp 202° C by HIO_4. With cooling and stirring, 48 mg of HIO_4 dissolved in 2 ml of water was added to a solution of 0.047 g of the diol in 2 ml of alcohol. The reaction mixture was left at room temperature for 24 hr. The reaction product was isolated in the usual way. Yield 0.039 g. The iodoform reaction was positive. The IR spectrum of the substance contained the frequencies of a γ-lactone (1764 cm^{-1}), an aliphatic ketone (1707 cm^{-1}) and a CO group in a five-membered ring (1724 cm^{-1}).

Oxidation of sieversinin with OsO_4. With cooling, a solution of 0.5 g of sieversinin in 4 ml of dioxane was added to a solution of 0.5 g of OsO_4 in 4 ml of dioxane. The mixture was kept at room temperature for 3 hr. Then 6 ml of a saturated solution of sodium sulfite was added to the reaction mixture. The dioxane was distilled off in vacuum. Ethereal extracts of the residue yielded 0.30 g of a substance with mp 160° C; after recrystallization, mp 161°–162° C (chloroform + petroleum ether).

Found, %: C 63.97; H 8.08. Calculated for $C_{15}H_{22}O_5$, %: C 63.83; H 7.81.

Oxidation of the substance with mp 161°–162° C by HIO_4. This process was carried out similarly to that described above. The oxidation product gave a positive iodoform reaction.

Oxidation of the substance with mp 161°–162° C by CrO_3. A solution of 4 mg of the substance in 40 ml of glacial acetic acid was treated with 10 mg of chromic anhydride. The mixture was left at room temperature for 24 hr. The oxidation product was isolated in the usual way. This gave a yellowish amorphous mass. The UV spectrum of the substance had λ_{max} 298 mμ.

All the microanalyses were carried out by E. A. Sokolova. The IR spectra were obtained by T. V. Bukreeva on an IKS-14 instrument with an NaCl prism using chloroform as the solvent. The NMR spectra of sieversinin were taken by E. I. Shul'gin and T. N. Timofeeva.

Summary

The essential oil and a petroleum ether extract of the epigeal part of Artemisia sieversiana Willd. have yielded a new sesquiterpene γ-lactone, sieversinin, with the composition $C_{15}H_{20}O_3$, mp 141°–142° C, $[\alpha]_D^{20}$ +57° which is evidently a stereoisomer of arborescin.

REFERENCES

1. J. Pliva, M. Horák, V. Herout, and F. Šorm, Die Terpene, Samml. der spektr. und physik, Konstanten, Berlin, 1, 1960.
2. B. B. Bates, Z. Čekan, V. Prochazka, and V. Herout, Tetrah. Lett., no. 17, 1127, 1963.
3. M. V. Nazarenko, Tr. BIN AN SSSR, ser. V, no. 8, 83, 1961.
4. M. Suchý, V. Herout, and F. Šorm, Coll. Czech. Chem. Commun., **29**, 1829, 1964.
5. A. Meisels and A. Weizmann, J. Amer. Chem. Soc., **75**, 2865, 1953.
6. J. Mazur and A. Meisels, Chem. Ind., no. 22, 492, 1956.

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