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DETERMINATION OF THE ABSOLUTE CONFIGURATION OF THE ASYMMETRIC CENTER AT C_{11} IN THE EUDESMANOLIDES

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UDC 547.314+582.998

It has been shown that it is possible to use the method of circular dichroism to determine the absolute configuration of the asymmetric center at C_{11} in the eudesmanolides. The orientations of the hydroxy group at C_1 and of the methyl group at C_4 in arabsin have been established.

In demonstrating the spatial structures of eudesmanolides, the determination of the absolute configuration of the asymmetric center at C_{11} is a fairly complex problem. The existing chemical method of determination, which is based on the treatment of the substance with phenyl selenide and sodium tetrahydroborate is laborious and requires the use of a large amount of material. It is also difficult to assign the signals of the proton at C_{11} from the NMR spectra.

Analysis of the results of circular dichroism (CD) measurements have shown that the sign of the Cotton effect (CE) in the 230-210 nm region, which is due to a n → π* transition in the lactone chromophore, is determined by two factors: the nature of the linkage of the lactone ring with ring B and the configuration of the asymmetric center at C_{11} in the lactone ring [1, 2]. Since natural sesquiterpene lactones of the eusdesmanolide type with the trans-linkage of rings A/B were considered, the influence of this factor on the parameters of the lactone CE was not taken into account.

Below we give the results of measurements of the circular dichroism of eudesmanolide:

Compound	Configuration	λ, nm	Δε	Compound	Configuration	λ, nm	Δε
Arabsin (I)	11R	283	+0.66	Tetrahydro-α-santonin (III)	11S	285	+0,83
		218	−0,59			215	−1,03
Arabsin (Ia)*		340	−0 26	Tetrahydro-β-santonin (IV)	11R	285	+0,91
		283	+0,54			215	−0,72
		238	+1.16	(Arsubin) (V)	11R	214	−0.41
		207	−2,17	(Artemin) (VI)	11S	218	+1,84
Arsanin (II)	11S	282	+0,64	(Artesin) (VII)	11S	218	+2,10
		215	+1,33	(Taurin) (VIII)	11S	294	−1,70
Arsanin (IIa)*		340	−0,28			223	+1,13
		283	+0,54			202	−5.70
		226	+2,10	(Ashurbin)(IX)	11S	223	+0.19
		207	−0,82	(Tetrahydroalantolactone (X)	11S	233	−0,10

*The CD measurements were made an hour after acidification.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 343-346, May-June, 1980. Original article submitted March 3, 1980.

0009-3130/80/1603-0254$07.50

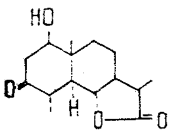
As these results show, in the case of the trans-linkage of rings B/C, all the lactones with an α-oriented CH_3 groups at C_{11} (11S configuration) have a positive CE in the 220 nm region, and compounds with the β-oriented CH_3 group (11R configureation) have a negative one. The observed laws agree well with the sector rule for a lactone chromophore [3].

Thus, if the nature of the linkage of the lactone ring to ring B is known, it is possible to determine the configuration of the asymmetric center at C_{11} from the circular dichroism characteristics.

We have available two linear eudesmanolides with the cis-linkage of the lactone rings: ashurbin (IX) and tetrahydroalantolactone (X), which are obtained by the reduction under analogous conditions with sodium tetrahydroborate of granilin and alantolactone, respectively. It is known that in (X) the methyl group at C_{11} has the β-orientation. In ashurbin, the orientation of the methyl group at C_{11} has not been established. On the basis of the fact that in the CD spectra of compounds (IX) and (X) Cotton effects identical in sign and similar in intensity are observed in the region of the lactone chromophore, we assumed that in ashurbin the methyl group at C_{11} has the β-orientation, as in tetrahydroalantolactone.

In the CD spectrum of arabsin (I) and in that of arsanin (II) there is a CE due to a n → π* transition in the carbonyl chromophore in the 280 nm region. The amplitudes of this CE in these two compounds is the same and, consequently, it may be assumed that the hydroxy group at C_1 and the methyl group at C_4 in arabsin have the same orientation as in arsanin, the stereochemistry of which has been established previously [4, 5].

The identity of the orientation of the OH groups in compounds (I) and (II) is also confirmed by their identical rates of dehydration. When ethanolic solutions of compounds (I) and (II) are acidified, a molecule of water is split out and a double bond conjugated with the carbonyl group is formed between C_1 and C_2 [5]. Under these conditions corresponding changes are observed in the CD spectra: the carbonyl CE shifts bathochromically to 340 nm and changes its sign, and additional Cotton effects due to π → π* and π → σ* transitions in the α,β-conjugated carbonyl chromophore appear in the 240 and 210 nm regions (Fig. 1). The latter are superposed on lactone Cotton effects of opposite sign, and therefore their intensities in arsanin and arabsin are different (see above). Measurement of the CD spectra one hour after acidification showed that the changes in the parameters of the n → π* carbonyl CE are similar for (I) and (II), i.e., the rates of their dehydration are practically the same and, consequently, the orientations of the hydroxy groups are identical (in this case, equatorial).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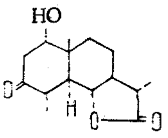
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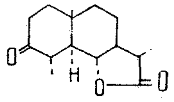
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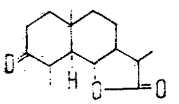
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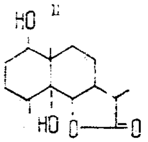
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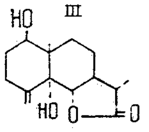
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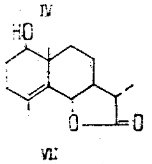
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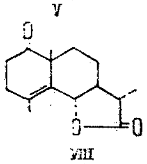
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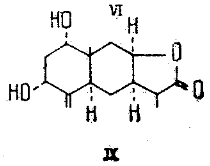
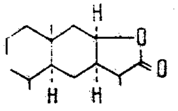

IX


X

The identity of the orientations of the methyl groups at C_4 in compounds (I) and (II) was confirmed by the passage to tetrahydro-β-santonin for (I) and to tetrahydro-α-santonin (II).

The intensity of the carbonyl CE in taurin is approximately five times higher than in ordinary 1-keto steroids [6] which is due to the interaction of the π-electrons of the carbonyl oxygen with the π-electrons of the $\Delta^{3(4)}$ bond.

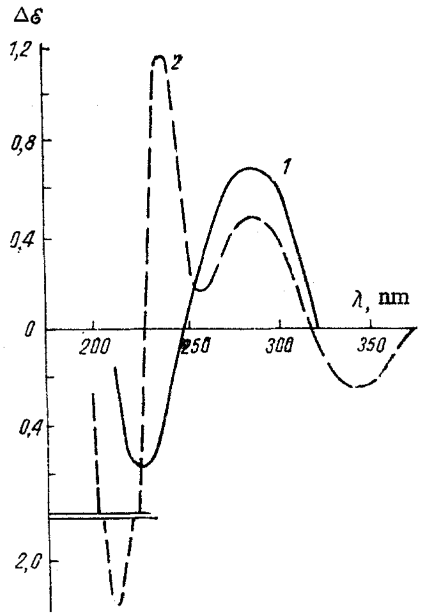


Fig. 1. CD spectrum of arabsin in CH_3OH (1) and $CH_3OH + HCl$ (2).

EXPERIMENTAL

The CD spectra were recorded on a JASCO J-20 spectropolarimeter. The concentration of the solutions was 1 mg/ml, and cell thicknesses of 0.5, 0.05, and 0.01 cm were used. The solvent was methanol. On acidification, a drop of concentrated hydrochloric acid was added to 3 ml of methanolic solution.

SUMMARY

1. It has been shown that the CD method can be used to determine the absolute configuration of the asymmetric center at C_{11} in eudesmanolides.

2. The orientations of the hydroxy group at C_1 and of the methyl group at C_4 in arabsin have been determined.

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