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CIRCULAR DICHROISM OF SOME STEROID ALKALOIDS

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In the present paper we consider the interconnection between the nature of the circular dichroism (CD) curves and the stereochemical features of steroid alkaloids: imperialine (I), eduardine (II), isogermine (III), veralodine (IV), and veralomidine (V). The structures of the compounds investigated have been established previously [1-6]. As can be seen from Fig. 1, for the C-nor-D-homosteroid alkaloids (I-III), there are two Cotton effects (CEs) in the CD spectra, in the 290 and 200 nm regions.

The sign and amplitude of the CE in the 290 nm region, due to a $n \rightarrow \pi^*$ transition in the carbonyl chromophore, confirms the trans-linkage of rings A/B in compounds (I-III) [7]. In the hydroxy ketone isogermine (III) the Cotton effect connected with the carbonyl chromophore is hypsochromically shifted in comparison with the usual position in 4-ketosteroids. Such a shift indicates the equatorial β orientation of the OH group at C_3. This is also confirmed by the fact that the intensity of the CE of (III) is almost the same as that of the unsubstituted 4-oxo compound [7]; in the case of an axial orientation of the OH group the amplitude of the CE should be considerably higher.

The CD spectra of compounds (I-III) contain, in addition to the long-wave CE, an intense CE in the 200 nm region caused by a $n \rightarrow \sigma^*$ transition in the C−N bond. This band disappears almost completely on acidification, which can be explained by the protonation of the nitrogen (Table 1). An analysis of the CD spectra of (I-III) has shown that the nature of the substituents of the closest asymmetric center at C_{20} has a substantial influence on the shortwave CE. Thus, the replacement of the hydrogen atom at C_{20} in (II) by a hydroxy group (I, III) causes a change in the sign of the CE. A negative CE in the 200 nm region may be connected with a 20R configuration (II) and a positive CE with a 20S configuration in compounds (I) and (III).

In the CD spectrum of veralodine (IV) (Fig. 2a) there are three CEs. Two of them, at 315 and 240 nm, are due to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions, respectively (R and K bands) in the α,β-unsaturated carbonyl chromophore, and the CE in the 205 nm region is connected with the lactam carbonyl. The nature of the CD spectrum of (IV) in the region of the R and K bands is the same as that of testosterone [7], which confirms the trans-linkage of rings BC and the $8\beta,9\alpha$ configuration in veralodine. A positive lactam CE at 205 nm is characteristic for the trans-linkage of rings E/F.

When a methanolic solution of (IV) was acidified, another (+)CE appeared in the CD spectrum at about 370 nm and the CE at 315 nm simultaneously decreased in intensity (see Fig. 2a). We assumed that in an acid medium dehydration takes place with the appearance of another double bond between C_6 and C_7 which increases the size of the system of conjugation and bathochromically shifts the $n \rightarrow \pi^*$ Cotton effect.

The CD spectrum of veralomidine (V) (Fig. 2b) is characterized by two negative CEs at 203 and 195 nm. On the acidification of a methanolic solution, the first CE decreases in intensity and the second remains unchanged, and on this basis the first CE is ascribed to a $n \rightarrow \sigma^*$ transition of the secondary amino group and the CE in the 195 nm region to a $\pi \rightarrow \pi^*$ transition of the C = C bond. By analogy with piperidine derivatives [8], the negative CE in the 203 nm region may be connected with the R configuration of the asymmetric center closest to the NH group, i.e., in the case of veralomidine, with the 22R configuration. In order to confirm the possibility of the use of the CE in the 200 nm region to determine the configuration of the asymmetric center

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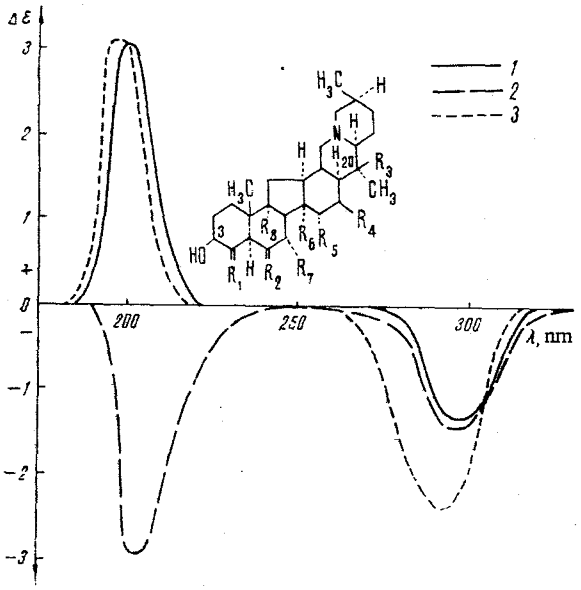

I. $R_1=H_2$; $R_2=O$; $R_3=OH$; $R_4-R_8=H$
II. $R_1=H_2$; $R_2=O$; $R_3=H$; $R_4-R_8=H$
III. $R_1=O$; $R_2=H_2$; $R_3=OH$; $R_4-R_8=OH$

Fig. 1. CD spectra of imperialine (I), eduardine (II), and isogermine (III) in CH_3OH.

TABLE 1

Compound	Methanol		Methanol+HCl		Dioxane	
	λ_{max}, nm	Δε	λ_{max}, nm	Δε	λ^*_{max}, nm	Δε
Imperialine (I)	294	−1,32	294	−1,32	298	−1,24
	200	+3,03	200	+0,20	—	—
Eduardine (II)	293	−1,43	293	−1,43	298	−1.25
	203	−2,46	200	−0,30	—	—
Isogermine (III)	282	−2,32	282	−2,30	284	−2,15
	195	+3,08	200	+0,25	—	—
Veralodine (IV)			370	+0,43	—	—
	315	−1,54	315	−1,06	330	−1.33
	240	+8,80	240	+10,09	235	+8,00
Veralomidine (V)	205	+9,50	205	+9,50	—	—
	203	−7,90	203	−6,05	—	—
	195	−8,25	195	−8,30	—	—

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*In dioxane a complex Cotton effect is observed in this region; Δε is given for the strongest maximum.

at C_{22}, we recorded the CD spectrum of tetrahydrosolasodine A, which has the 22S configuration [9]. As was assumed, in the CD spectrum of tetrahydrosolasodine at 205 nm there is a positive CE, confirming the 22S configuration.

In dioxane the nature of the circular dichroism of the compounds under consideration scarcely changes, and it is only possible to detect a slight bathochromic shift for the $n \rightarrow \pi^*$ Cotton effects.

EXPERIMENTAL

The CD spectra were recorded on a JASCO J-20 spectropolarimeter. The concentration of the solutions was 1 mg/ml, and the cell thicknesses were 0.5, 0.2, and 0.05 cm. Methanol and dioxane were used as solvents. For acidification, one drop of concentrated hydrochloric acid was added to 5 ml of a methanolic solution of a base. The CD measurements were made one hour after the addition of the acid.

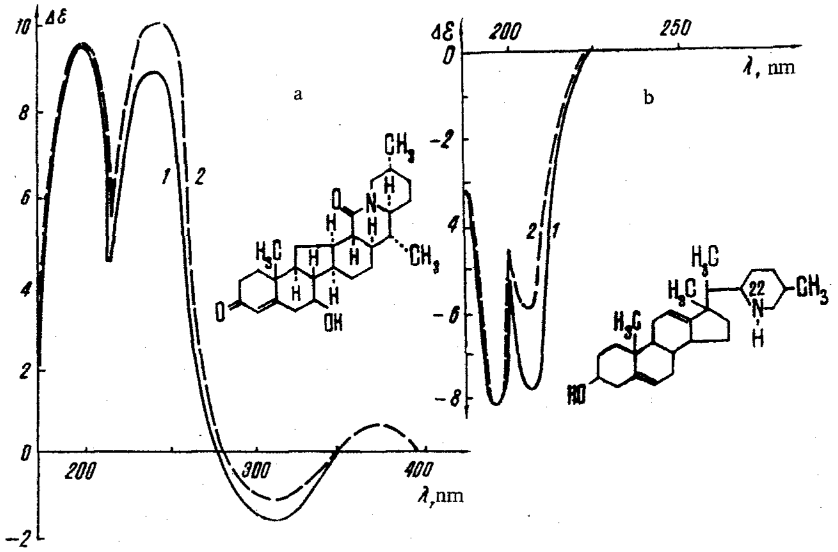

Fig. 2. CD spectra of veralodine (a) and veralomidine (b) in CH_3OH (1) and CH_3OH + HCl (2).

SUMMARY

1. The trans-linkage of rings A/B in compounds (I-III) and of rings B/C and E/F in veralodine and the equatorial orientation of the OH group at C_3 in isogermine has been confirmed by CD spectroscopy.

2. A relationship has been established between the nature of the substituents and the configurations at C_{20} and the sign of the CE in the 200 nm region for compounds (I-III).

3. The 22R configuration has been established for veralomidine.

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