CIRCULAR DICHROISM OF VERALOSIDINE AND ITS DERIVATIVES

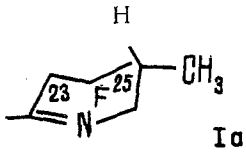
G. P. Moiseeva, R. Shakirov,
M. R. Yagudaev, and S. Yu. Yunusov

UDC 547.944/945

The structure of veralosidine (I) has been shown previously by chemical transformations and by IR and NMR spectroscopy [1, 2]. On the basis of the similarity of the IR spectra of the diketones from tetrahydrosolasodine and tetrahydroveralosidine, veralosidine was ascribed to the 25R series [2]. However, the configuration of the asymmetric center at C_{25} was not shown strictly.

In order to determine unambiguously the configuration of the asymmetric center at C_{25} we have considered the circular dichroism (CD) spectra of veralosidine and its derivatives. In the 250-230 nm region, cyclic azomethines have a Cotton effect (CE) which is connected with the $n \rightarrow \pi^*$ transition in the C = N chromophore. The sign of this CE is determined by the conformation of the azomethine ring [3]. The azomethine rule has been confirmed by numerous examples and, in particular, it has been used for steroid alkaloids analogous to veralosidine [4, 5]. It has been shown [4] that the conformation of the azomethine ring and the configuration of the asymmetric center in this ring at C_{25} are interconnected, and if the conformation of the ring is known it is possible to determine the configuration of the C_{25} center. It has been established that compounds belonging to the 25S series have a negative CE and those belonging to the 25R series a positive CE.

In the CD spectrum of veralosidine (Fig. 1), a negative CE can be seen at 235 nm, and on this basis it can be stated that its azomethine ring is present in conformation (Ia) and it has the 25S configuration.



Ia

We have also recorded the CD spectra of two other veralosidine derivatives: Δ^4-veralosidin-3-one (II), and O,O'-diacetylveralosidine (III). The spectra obtained have been compared with the CD spectrum of the product of the acetolysis of solasodine – O,O'-diacetylpseudosolasodine (IV) – a known alkaloid belonging to the 25R series [2]. As was assumed, in the region of absorption of the azomethine chromophore the CD spectrum of (IV) shows a positive Cotton effect, while the spectra of (II) and (III) show negative effects. Thus, the conformation of ring F and the configuration of the C_{25} center in the veralosidine derivatives (II) and (III) are opposite to that of the solasidine derivative (IV), i.e., compounds (II) and (III) belong to the 25-S series. As can be seen from Table 1, the intensity of the negative azomethine Cotton effect in (II) is smaller than in (I) and (III) since it overlaps with the positive Cotton effect of the $\pi \rightarrow \pi^*$ transition of the α,β-unsaturated carbonyl group. The negative Cotton effect at 314 nm connected with the $n \rightarrow \pi^*$ carbonyl transition [5] shows the $8\beta,9\alpha$ configuration and the trans linkage of rings B/C in the ketone (II), and consequently also in the initial veralosidine.

On acidification, another difference can be seen in the CD spectra between the 25S compounds and O,O'-diacetylpseudosolasodine. On the CD curve of (IV), the CE is shifted hypsochromically and changes its sign, while in veralosidine and its acetolysis product only a hypsochromic shift of the CE to 208 nm is observed.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 623-625, September-October, 1976. Original article submitted March 11, 1976.

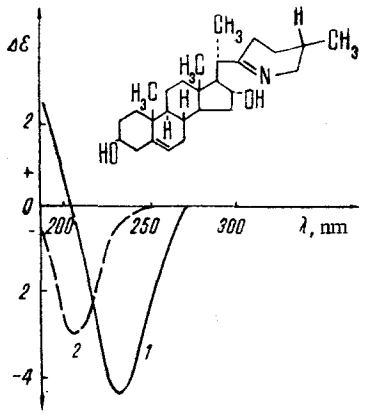


Fig. 1. CD spectrum of veralosidine in CH_3OH (1) and CH_3OH + HCl (2).

TABLE 1

Compound	Methanol		Methanol + HCl	
	λ_{max}, nm	Δε	λ_{max}, nm	Δε
Veralosidine (I)	235	−4,34	208	−3,03
Δ^4-Veralosidin-3-one (II)	315	−1,40	315	−1,40
	242	−2,78	242	+3,18
	210	+8,35	215	+7,40
O,O'-Diacetylveralosidine (III)	237	−5,50	208	−4,80
O,O-Diacetylpseudosolasodine (IV)	237	+2,08	215	−1,79
Veralosine (V)	237	−5,45	209	−4,,2
Veralosinine (VI)	237	−5,40	209	−4,70
Veralosidinine (VII)	242	−2,06	208	−4,22

The analogous change in the CD spectrum of (II) is not so clearly pronounced because of the superposition of the Cotton effects of the α,β-unsaturated carbonyl group. The appearance of a CE in the 208-nm region may be connected either with salt formation or with the migration of the double bond in the azomethine ring into the C_{22}-C_{23} position [2]. The migration of the double bond in ring F should form an olefinic proton. However, in the NMR spectrum of (I) obtained in CD_3OD solution with the addition of DCl no positive signal of the olefinic proton was detected. Consequently, acidification leads only to salt-formation.

Veralosine (V) and veralosinine (VI), for which a link with veralosidine has been established chemically [2, 7], and in the CD spectra of which a negative CE is observed at 237 nm, can also be assigned to the 25S series. In the case of veralosidinine (VII) [8] no chemical transition to (I) has been effected, but the presence in the CD spectrum of (VII) of a negative CE at 242 nm which shifts to 208 nm on acidification shows the 25S configuration in this compound.

EXPERIMENTAL

The CD spectra were recorded on a JASCO J-20 spectropolarimeter. The concentration of the solutions was 1 mg/ml and the cell thickness 0.05 cm. Methanol was used as the solvent. For acidification, a drop of concentrated hydrochloric acid was added to 2 ml of methanolic solution. The CD measurements were made an hour after the addition of the hydrochloric acid.

SUMMARY

On the basis of their CD spectra, the alkaloids veralosidine, veralosine, veralosinine, and veralosidinine have been assigned to the 25S series.

LITERATURE CITED

1. A. M. Khashimov, R. Shakirov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 339 (1970).
2. A. M. Khashimov, R. Shakirov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 779 (1971).
3. P. Crabbé, Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry, Holden−Day, San Francisco (1965).

4. H. Ripperger, K. Schreiber, and G. Spatzke, Tetrahedron, 21, 1027 (1965).
5. G. Adam, K. Schreiber, J. Tomko, and A. Vasson, Tetrahedron, 23, 167 (1967).
6. L. Velluz, M. Legrand, and M. Grosjean, Optical Circular Dichroism, Academic Press, New York (1965).
7. A. M. Khashimov, R. Shakirov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 343 (1970).
8. R. Shakirov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 501 (1973).

ALKALOIDS OF Reseda luteola

K. L. Lutfullin, M. M. Tadzhibaev,
U. A. Abdullaev, V. M. Malikov,
and S. Yu. Yunusov

UDC 547.94:547.78

Plants of the genus Reseda growing in the territory of the USSR have not previously been studied for their alkaloid content [1]. There is information on the isolation of sulfur-containing bases from some species of this genus [2]. We have previously reported the isolation of two new alkaloids – resedine, $C_9H_9NO_2$, and resedinine, C_9H_9NOS – from R. luteola L. [3]. We later developed methods for isolating and separating the combined alkaloids, and also obtained new chemical and spectral information confirming the structures of these alkaloids and their transformation products.

From the plant collected in the flowering period in the Samarkand oblast by the usual chloroform extraction we obtained a comparatively low yield (0.02%) of total alkaloids. The bulk of the alkaloids did not pass into the chloroform from the raw material, and another part was not extracted by organic solvents because of its high solubility in water, and therefore the raw material was extracted with a 1% solution of sulfuric acid. The extract was passed successively through KU-1 and KU-2 cation-exchange resins. The alkaloids were desorbed from the resins by means of an ethanolic solution of ammonia. The yield of combined alkaloids was 0.24%.

By separating the combined alkaloids according to their solubilities in organic solvents and by chromatography on a column of silica gel, we isolated four bases: resedine, resedinine, phenyl-β-naphthylamine, and β-hydroxyphenylethylamine.

The chemical transformations of resedine (I) and resedinine (II) gave a series of products which confirmed the structures proposed previously for these alkaloids [3]. The reduction of (I) in the presence of Raney nickel gave a base (III). The mass spectrum of (III) had the peaks of ions with c m/e 121 M^+ (3.3%) 91 (26.3%), 79 (2%), 77 (6%), 30 (100%) which agrees completely with the mass spectrum of phenylethylamine [4].

To confirm the structure and establish the site of attachment of the phenyl radical to the heterocyclic ring of resedine we reduced (I) with $LiAlH_4$ and obtained a mixture of products from which we isolated a liquid base (IV). The IR spectrum of (IV) contained absorption bands at 3200-3400 cm^{-1} (active hydrogen) and 710 and 770 cm^{-1} (monosubstituted benzene ring). The NMR spectrum of (IV) showed the signals of protons at 713 ppm (5 H, singlet, monosubstituted benzene ring), 4.60 ppm (1 H, triplet, $Ar-\underset{\underset{O-}{|}}{CH}-CH_2-$) 4.37 ppm (2 H, broadened singlet, =NH, OH), 2.40 (2 H, doublet, $=CH-\underline{CH_2}-$), and 2.18 ppm (3 H, singlet, $N-CH_3$). The mass spectrum of (IV) had the peaks of ions with c m/e 151 M^+ (10%), 107 (20%), 105 (40%), 79 (90%), 77 (95%), 44 (100%). An analysis of the spectra of (IV) leads to the structure of β-(hydroxyphenyl)-N-methylethylamine. The acetylation of (IV) with acetic anhydride in the presence of pyridine gave a O,N-diacetyl derivative (V), M^+ 235. In the IR spectrum of (V), the absorption band of active hydrogen had disappeared and the absorption bands of a carbonyl group had appeared at 1750 and 1670 cm^{-1}, which also confirms the structure for (IV) given above.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. M. I. Kalinin Andizhan Medical Institute. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 625-630, September-October, 1976. Original article submitted April 6, 1976.