OPTICAL ROTATORY DISPERSION CURVES OF THE QUINOLIZIDINE ALKALOIDS

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The investigation of the absolute configurations and conformations of various amides of the quinolizidine series by the optical rotatory dispersion (ORD) method gives valuable information not accessible by the use of other physical methods. In a preceding paper it was shown that the sign of the Cotton effect correlates with the configuration of an asymmetric carbon attached to a nitrogen atom forming part of a lactam grouping [1].

The present paper gives the results of a comparative investigation of the ORD curves of saturated amides and alkaloids containing the α-pyridone chromophore. The ORD curves have been recorded (on a Cary-60 instrument in a cell 5 mm thick using 1-2 mg of substance) of the following compounds: (−)-cytisine (I), (−)-N-methylcytisine (II), (−)-N-acetylcytisine (III), (−)-N-butylcytisine (IV), (−)-dicytisine-N,N'-ethane (V), (−)-alteramine (VI), (−)-dihydroalteramine (VII), (−)-leontidine (VIII), (−)-thermopsine (IX), (−)-anagyrine (X, methiodide), (−)-hexahydroalteramine (XI), (−)-tetrahydrocytisine (XII), (−)-tetrahydroleontidine (XIII), (−)-hexahydrodes-N-methylleontidine (XIV), (+)-aphylline (XV), (+)-oxosparteine (XVI), (−)-α-isolupanine (XVII), (+)-aphyllidine (XVIII), and (−)-matridine (XIX).

The UV absorption spectra of α-pyridone-containing alkaloids are characterized by two maxima, at 234 and 310 nm, with fairly high extinction coefficients: in the hydrogenation products there is absorption between 205 and 210 nm [2]. In spite of the fact that all the compounds possess a very low light permeability, because of the high rotation in the region of the optically active bands, it has been possible to record the curves down to 190 nm. Methanol and water were selected as universal solvents. On comparing the curves obtained in the different solvents, no influence of the polarity of the medium was observed.

Alkaloids (I)-(X) give curves (Figs. 1-3) with two Cotton effects (negative at about 310 nm and positive at 230 nm), corresponding to the absorption maxima in the UV spectra.

Shifts in the UV spectra due to the structure of the molecules are practically absent, and in the ORD curves they amount to ±6 nm. The most hypsochromic shift is found in (III), and the most bathochromic in (VI). The presence of substituents in ring C affects its conformation, which leads to a change in the amplitude of the Cotton effect of the compounds studied. In the N-alkyl homologs of (I) the magnitude of the rotation changes slightly with an increase in the length of the hydrocarbon chain. The greatest contribution to the rotation is made by the appearance of a N-acetyl group, as a result of pronounced deformation of ring C. In these compounds the influence of substituents on the amplitude was the same for both extrema. Only in case (III) did the amplitude of the second extremum rise sharply. Matridine (XIX) possesses a smooth ORD curve down to 200 nm (Fig. 4), which is due to the absence of a chromophore absorbing in a region accessible for study. Consequently, the absorption at about 220 nm in compounds (I)-(IX) may be ascribed to the n→δ* transitions of the C−N bonds of the nitrogen atom in position 2.

In the spectra of (VIII)-(X), the nature of the curves in the 220 nm region and beyond changes sharply according to the configuration of the CD rings. Some difference can be observed on comparing the width of the Cotton effects. The width of the first extremum is 47-52 nm and that of the second is 20-23 nm. The influence of the skeletal effect on the width of the extrema in these compounds is not great; the greater

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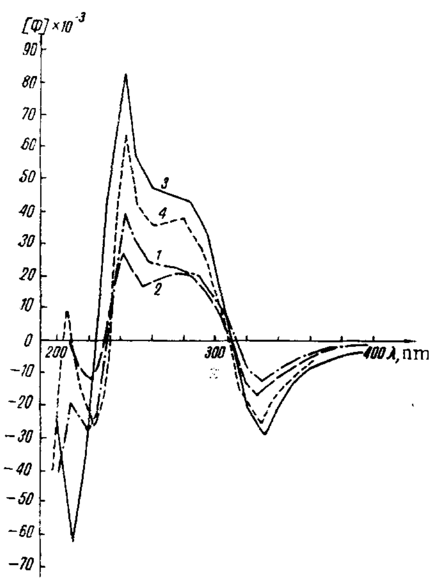

Fig. 1

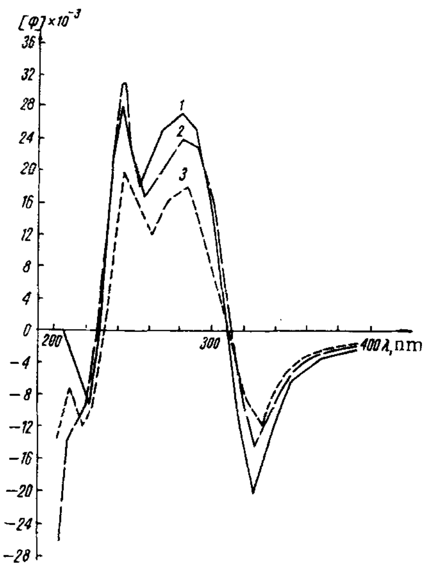

Fig. 2

Fig. 1. ORD curves of (−)-cytisine (I) (1), (−)-N-methylcytisine (II) (2), (−)-N-acetylcytisine (III) (3), and (−)-dicytisine-N,N'-ethane (V) (4).

Fig. 2. ORD curves of (−)-N-butylcytisine (IV) (1), (−)-alteramine (VI) (2), (−)-dihydroalteramine (VII) (3).

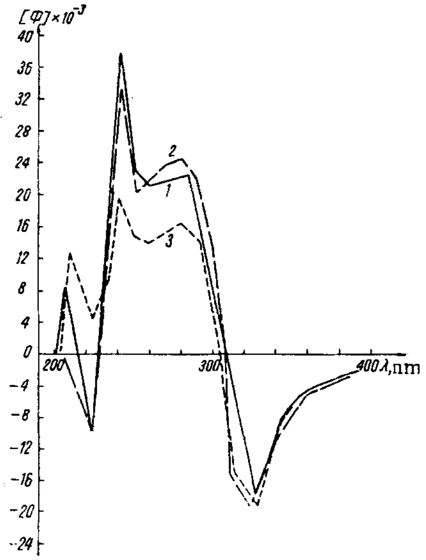

Fig. 3

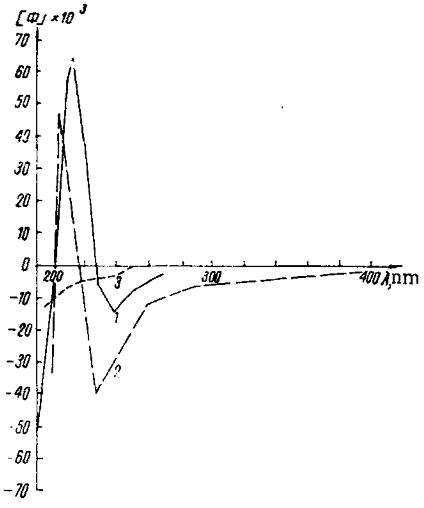

Fig. 4

Fig. 3. ORD curves of (−)-leontidine (VIII) (1), (−)-thermopsine (IX) (2), and (−)-anagyrine methiodide (X) (3).

Fig. 4. ORD curves of (−)-tetrahydroleontidine (XIII) (1), (−)-hexahydrodes-N-methylleontidine (XIV) (2), and (−)-matridine (XIX) (3).

width of the second extremum in (III) can be explained by the additivity of the contribution to the amplitude of the Cotton effect made by the carbonyl of the N-acetyl group. The agreement of the signs of the Cotton effect in the curves of the α-pyridone derivatives (I)-(V) and in (IX) and (X) shows the similar arrangement of the bridge asymmetric carbon atoms that was shown previously by chemical reactions [3, 4].

With a change in the concentrations of the solutions, the specific rotations of (I) and (II) change sharply. In the curves of (I) obtained at various concentrations in methanol, a Cotton effect is absent, and

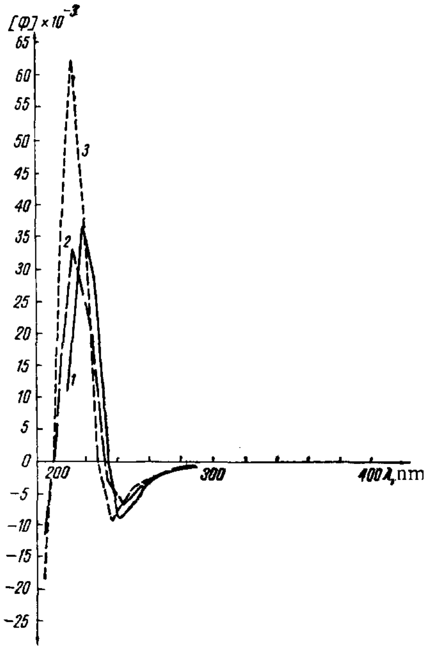

Fig. 5. ORD curves of (−)-tetrahydrocytisine (XII) (1), (−)-hexahydroalteramine (XI) (2), and (−)-α-isolupanine (XVII) (3).

therefore it is possible to determine it quantitatively by the spectropolarimetric method.

In spite of the fact that optically active absorption in the saturated compounds (XII)-(XVII) appears in the short-wave part of the spectrum, the ORD method gives more interesting results for these than for the α-pyridones. The signs of the Cotton effects in these compounds also show the configurations of the carbon atoms attached to the lactam nitrogens, regardless of whether the carbonyl is in the outer or the inner ring, which is illustrated by the similar negative Cotton effects of the alkaloids (XV) and (XVII), which have the 6S configuration [2-4]. In compound (XVI), where C_{11} has the R configurations [5], the curve of the Cotton effect is positive. Depending on the configurations at C_6 and C_{11}, the conformations of rings AB or CD change. This is clearly reflected in the magnitude of the Cotton effect and the width of the extrema. The highest values are found for trans-quinolizidones with the carbonyl in the outer ring. The presence of a double bond in (XV) at C_5-C_6 leads to the disappearance of the asymmetric C_6, the sign of the Cotton effect acquiring the opposite rotation.

Thus, by comparing the ORD curves of various amides and α-pyridones of the quinolizidine series, it is possible to determine the position of the carbonyl group and the absolute configurations of the adjacent asymmetric centers.

The curves of leontidine and alteramine have similar shapes and similar signs to the α-pyridone derivatives. Differences in the magnitude and width of the Cotton effect are due to a skeletal effect. This makes it possible to deduce the similar R configurations of the C_7, C_9 bridge carbon atoms in leontidine and alteramine.

On comparing the ORD curves of saturated amides obtained by the hydrogenation of the tricyclic alkaloids (I)-(V) with the tetracyclic alkaloids, again the dependence of the sign of the Cotton effect on the C_6 configuration is observed (Figs. 4 and 5). However, the shift in the optically active absorption as a function of the structure of the compounds is comparatively greater than in the α-pyridones, amounting to 20 nm. The appearance of a fourth ring in the skeleton of (XII), i.e., in the spectrum of (XIII), leads to a marked increase in the amplitude of the rotation: the value of the peak rises far more strongly than that of the trough. The cleavage of the $C_{11}-N_{15}$ bond with the formation of a ten-membered ring (XIV) causes a displacement of the ORD curves to negative values of the rotation, which can be explained by a change in the skeletal effect.

In the IR spectrum of leontidine absorption bands appear between 2800 and 2700 cm^{-1}, which shows the trans linkage of the indolizidine system [6]. A consideration of models of leontidine and tetrahydroleontidine show that a trans linkage of the C/D rings leads to the 11S, 15S configuration. Consequently, leontidine has the 7R, 9R, 11S, 15S configuration, and tetrahydrodeoxyleontidine the 6S, 7R, 9R, 11S, 15S configuration.

The presence in the IR spectra of alteramine and its hydrogenation products of the absorption bands of α-trans-axial hydrogens and the conversion of allylcytisine into alteramine on methylation and into leontidine on cyclization [7] permit the same configuration to be adopted for them.

SUMMARY

The possibilities of the use of ORD methods for determining the absolute configuration of amides and of α-pyridone alkaloids have been studied and demonstrated.

LITERATURE CITED

1. S. Iskandarov, D. Dzh. Kamalitdinov, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 7, 174 (1971).
2. S. Iskandarov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 6, 494 (1970).

3. S. Okuda, K. Tsuda, and H. Kataoka, Chem. Ind. (London), 1961, No. 43, 1751.
4. S. Okuda, K. Tsuda, and H. Katoaka, Chem. Ind. (London), 1961, No. 29, 1115.
5. R. H. F. Manske, The Alkaloids, Vol. IX, Academic Press, New York (1967), p. 175.
6. F. Bohlmann, Ber., 91, 2157 (1958).
7. S. Iskandarov, R. A. Shaimardanov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 7, 631 (1971).