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ISOMERIZATION OF THE HYDROCHLORIDES OF SOME ALKALOIDS OF THE MATRINE SERIES

A. I. Begisheva, Kh. A. Aslanov, A. S. Sadykov, and V. B. Leont'ev

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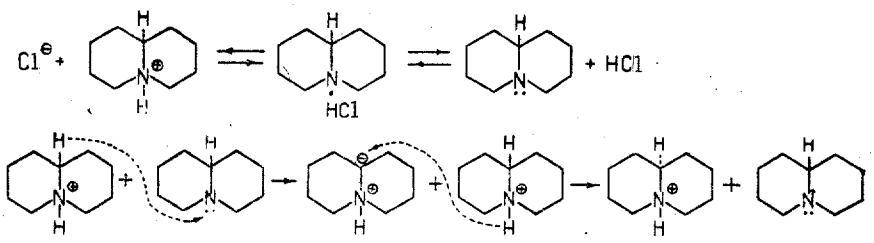
Thermal treatment of the chloride of aphylline (cis-A/B, cis-C/D) gives α-isoaphylline, the trans-trans isomer [1,2].

We have fused the hydrochlorides of allomatrine, matrine, sophoridine, isosophoridine, and their oxygen-free derivatives—allomatridine, matridine, sophoridane, and isosophoridane—in an atmosphere of nitrogen at a constant temperature for 30 min.

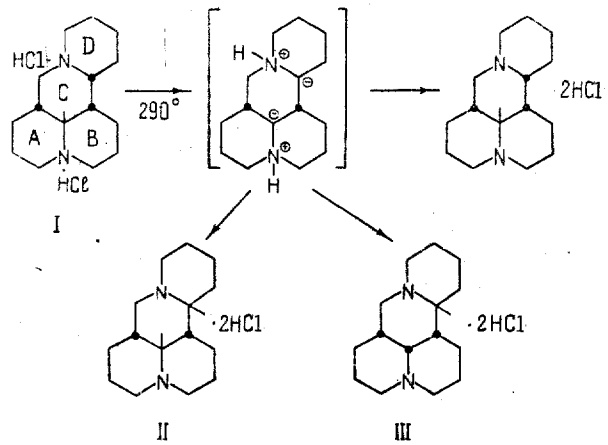
Isomerization took place in those cases where the molecule contained a cis-quinolizidine system capable of forming a salt; in the other cases the starting materials were recovered. In explaining the mechanism of isomerization under the given conditions, we assumed, in the first place, that when the hydrochlorides of the alkaloids were fused not only did dissociation to ions take place in the melt but also dissociation into the acid and the free base, which acts as a hydrogen acceptor in the isomerization reaction and, in the second place, that the hydrochlorides of the alkaloids can be regarded as quaternary ammonium salts where one R=H. Since no cleavage of the molecule took place in our experiments, we consider that the isomerization takes place with the formation of carbanions [3,4] as intermediate products.

On the basis of what has been said above, the mechanism of the isomerization of the salt of these quinolizidine alkaloids is represented in the following way:



The internal salt formed, a nitrogen ylide, is characterized by high reactivity and a tendency to the rapid addition of a proton, which may approach the carbanion both from the front and from the back of the plane of the reaction center [5].

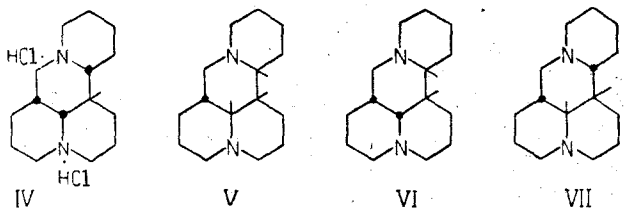
When two active centers are present, for example in sophoridine (I), the formation of several isomers is observed.



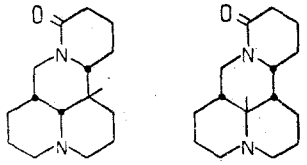
When protons add to both active centers of the carbanions from the side from which they were in the original position, the original sophoridine is formed; when they add to C_{11} from the rear and to C_{16} from the front allomatridine (II) is formed, while the addition at both points from the opposite side in relation to the initial position leads to the formation of matridine (III). This process evidently takes place as a result of the conversion of the carbanion through the chair ⇄ boat forms of rings C and D.

If this method is applied to the possible isomerization of the hydrochloride of isosophoridane (IV), the formation of the three unknown isomers of the cis-series V-VII may be assumed.

As can be seen, isomerization takes place through one of these products which isomerizes in its turn, leading to a more stable isomer, allomatridine, which we isolated from the reaction products together with the initial isosophoridane.



IV V VI VII



VIII IX

In the case of isosophoridine (VIII) we obtained sophoridine (IX) (cis-C/D). This is probably due to the presence of a lactam carbonyl in ring D of isosophoridine which, as a result of hindrance to free conversion, leads to a cis-C/D linkage, i.e., to sophoridine.

No.	Substance	Configuration	ΔE, kcal/mole	No.	Substance	Configuration	ΔE, kcal/mole
1		trans-A/B trans-A/C trans-B/C	0	7	Isosophoridane	cis-A/B cis-A/C trans-B/C trans-C/D	6.2
2	Hexahydrojulolidine	trans-A/B cis-A/C cis-B/C	3.6	8	Cis isomer	cis-A/B trans-A/C cis-B/C trans-C/D	6.2
3		cis-A/B cis-A/C trans-B/C	6.2	9	Trans isomer	trans-A/B cis-A/C cis-B/C cis-C/D	8.9
4	Allomatridine	trans-A/B trans-A/C trans-B/C trans-C/D	0	10	Cis isomer	cis-A/B cis-A/C trans-B/C cis-C/D	11.5
5	Matridine	trans-A/B cis-A/C cis-B/C trans-C/D	3.6	11	Trans isomer	cis-A/B trans-A/C cis-B/C cis-C/D	11.5
6	Sophoridane	trans-A/B trans-A/C trans-B/D cis-C/D	5.3				

Note. ΔE given with respect to the all-trans isomers.

We have considered the relative energies of the isomers of julolidine and matridine, taking the energy of the skew butane interaction as 0.9 kcal/mole [6] and taking into account the electronic influence of the unshared pair of the nitrogen on the α-trans-axial C—H-bond—$E_{\sigma\varepsilon}$, 2.2 kcal/mole—and its angular effect due to its "size" (1.8 kcal/mole for cis-quinolizidine and 3.6 kcal/mole for trans-quinolizidine) [7-9] (table).

It follows from the table that the hexahydrojulolidines can be arranged in order of stability as follows: 1 > 2 > 3, which agrees with the results of previous experiments [10,11], and the matridines in the order 4 > 5 > 6 ≫ 7, 8 > 9 ≫ ≫ 10, 11. The isomers 10 and 11 of the cis series differ from allomatridine by more than 10 kcal/mole. This permits the conclusion that the existence of such configurations is possible only when factors lowering the free energy of the molecule are present.

Conclusions

The conversions of sophoridane into allomatridine and matridine, of isosophoridane into allomatridine, and of isosophoridine into sophoridine have been effected. A mechanism has been proposed for the thermal isomerization of the hydrochlorides of the quinolizidine alkaloids.

REFERENCES

1. A. S. Labenskii, ZhOKh, **28**, 517, 1958.
2. A. I. Ishbaev, A. S. Sadykov, and Kh. A. Aslanov, ZhOKh, **35**, 194, 1965.
3. W. Haegi, Usp. khim., **25**, 903, 1956, [translated from Bull. Soc. Chim., no. 4, 581, 1955].
4. G. Wittig, Usp. khim., **26**, 1142, 1957, [translated from Experientia, **12**, 41, 1956].
5. D. H. R. Barton and C. H. Robinson, J. Chem. Soc., 3045, 1954.
6. W. S. Johnson, J. Am. Chem. Soc., **75**, 1498, 1953.
7. T. M. Moynehan, K. Schofield, R. A. I. Jones, and A. R. Katritzky, J. Chem. Soc., 2637, 1962.
8. N. L. Allinger and J. C. Tai, J. Am. Chem. Soc., **87**, 1227, 1965.
9. N. L. Allinger, J. G. D. Carpenter, and F. M. Kakowski, J. Am. Chem. Soc., **87**, 1232, 1965.
10. M. Potiva and V. Prelog, Helv. chim. acta, **32**, 621, 1949.
11. F. Bohlmann, Ber., **91**, 2167, 1958.

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Tashkent State University