Chemistry

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Abstract

Full Text

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Some Questions of the Stereochemistry of Quinolizidine Alkaloids

Despite the existence of numerous works (^{1}) in the field of quinolizidine alkaloids, questions of the stereochemistry, and especially the conformation, of this group of bases continue to attract the attention of investigators.

Most quinolizidine alkaloids contain a lactam group in their molecule and, depending on its position, behave differently toward various reagents. In the present work an attempt has been made to clarify the reason for the behavior of certain alkaloids of the quinolizidine group in connection with their conformation.

The action of caustic potash, sulfuric acid, and sodium amide on a series of alkaloids containing a lactam group was studied. Reactions with sulfuric acid and caustic potash were carried out by heating the mixture at 90—100° for 20-25 hr; with sodium amide the analogous reaction was carried out by boiling a mixture of the alkaloids and reagent in toluene solution for 4-5 hr. For the experiments, alkaloids of three types were taken: 1) alkaloids in which the lactam group is in the outer ring (matrine I and α-isolupanine IIa); 2) alkaloids with the lactam group in the inner ring of trans-quinolizidine (aphylline IIb and α-isoaphylline III), and 3) alkaloids with the lactam group in the inner ring of cis-quinolizidine (oxopachycarpine IIv and oxoaphylline IIg).

[chemical structures]

I

II

a) $R' = O,\ R''R''' = H_2$
b) $R'' = O,\ R'R''' = H_2$
c) $R''' = O,\ R'R'' = H_2$
d) $R''R''' = O,\ R' = H_2$

III

The data obtained are given in Table 1.

Table 1

Alkaloids	KOH 15% (alcohol): taken, g	KOH 15% (alcohol): amino acid, %	KOH 15% (alcohol): recovered substance, %	H_2SO_4 40%: taken, g	H_2SO_4 40%: amino acid, %	H_2SO_4 40%: recovered substance, %	$NaNH_2$: starting substance, g: base	$NaNH_2$: starting substance, g: sodium amide	$NaNH_2$: starting substance, g: toluene	$NaNH_2$: amino acid, %	$NaNH_2$: recovered substance, %
Matrine	3	71,2	9,30	5	78,5	7	2	1	20	–	86
α-Isolupanine	2	66,5	12	2	89,12	–	2	1	20	–	93
Aphylline	3	15,16	75,7	5	90	6	2	1	20	86,92	–
Aphyllidine	3	10,8	84	5	81,02	5,4	2	1	20	79,44	–
α-Isoaphylline *	–	–	–	2	79,81	7,5	–	–	–	–	–
Oxopachycarpine	3	–	80	5	–	91,8	2	1	20	–	83,2
Oxoaphylline **	–	–	–	2	77,1	16	–	–	–	–	–

* α-Isoaphylline was obtained by us by dehydrogenation of aphylline with subsequent hydrogenation of Δ^{11-12}-dehydroaphylline, and also by isomerization of aphylline hydrochloride.

** Oxoaphylline (IIg) has 2 lactam groups, located in the inner ring of cis-, and also trans-quinolizidine.

The data of Table 1 show that alkaline saponification is not characteristic of all quinolizidine alkaloids with a lactam carbonyl. Under these conditions only the lactam group located in the outer ring of quinolizidine systems (matrine and α-isolupanine) is readily saponified.

Interesting data were obtained under the action of 40% sulfuric acid. If, in the alkaloid molecule, the lactam group is located in the outer ring, it is readily opened with formation of the corresponding amino acids, and the latter readily cyclize, forming the original base. This is evidently due to the fact that there are no steric hindrances here. When the lactam group is located in the inner ring of the trans-quinolizidine system of the alkaloid, it is opened with greater difficulty, and the amino acid obtained cyclizes to the original base only after additional treatment. If, however, the lactam group is located in the inner ring of cis-quinolizidine, opening of the latter does not occur. These facts agree well with the literature data ([2–4]).

Reaction scheme with quinolizidine structures labeled IV, V, and VI, showing transformations involving $NaNH_2$, NH_3, and H_2O.

Figure 1: Reaction scheme with quinolizidine structures labeled IV, V, and VI, showing transformations involving $NaNH_2$, NH_3, and H_2O.

Table 2

Alkaloids	Oxidizing agent	Compound obtained
Pachycarpine	$K_3Fe(CN)_6$	17-Oxopachycarpine (²)
Aphylline	$K_3Fe(CN)_6$	17-Oxoaphylline
Lupanine	$K_3Fe(CN)_6$	17-Oxolupanine (⁵)
Anagyrine	$Ba(MnO_4)_2$	17-Oxoanagyrine (⁶)
α-Isosparteine	$K_3Fe(CN)_6$	Not oxidized
α-Isoaphyllidine	$K_3Fe(CN)_6$	Not oxidized
α-Isolupanine	$K_3Fe(CN)_6$	Not oxidized
Thermopsine	$K_3Fe(CN)_6$	Not oxidized

When the conformational formulas of alkaloids with a lactam carbonyl in the trans-(IIb)- and cis-(IIc)-quinolizidine nucleus are considered, it is seen that the carbonyl in the cis-quinolizidine nucleus is significantly screened by the piperidine ring, as a result of which it is attacked with difficulty by nucleophilic reagents. In the first case the carbonyl is in a favorable position for the action of nucleophilic reagents.

A peculiar regularity was observed by us in the oxidation of certain alkaloids of the quinolizidine series with introduction of a lactam carbonyl into the molecule: a carbonyl that is readily opened during saponification is formed with difficulty during oxidation and, conversely, a lactam carbonyl that is readily formed by oxidation is saponified with difficulty. The results of the oxidation are given in Table 2.

Interesting and unexpected results were obtained under the action of sodium amide on matrine and α-isolupanine. Although these alkaloids react very vigorously with sodium amide, the reaction products, on treatment with water, are converted back into the original bases, whereas aphylline and aphyllidine form the corresponding acid amides (⁷).

From this it may be concluded that the sodium derivatives of the acid amide (IV), in the process of decomposition by water and as a result of tautomeric rearrangement (V, VI), readily cyclize with formation of the original base.

Confirmation of this supposition is provided by the fact that in the IR spectrum of the products of interaction of the indicated bases with sodium amide, the characteristic band for the lactam group (1620–1640 cm^{-1}) is absent. In addition, under the action of ammonia on the ethyl ester of matrine acid, it is not the acid amide that is formed, but matrine. The ethyl ester of aphyllinic acid, under the action of ammonia, is converted into the amide in quantitative yield.

Thus, as a result of the work carried out, it has been established that the lactam group located in the outer ring of quinolizidine is the most susceptible to the action of acids, alkalis, and sodium amide. More difficult to subject to the action of these reagents is the lactam group located in the inner ring of trans-quinolizidine. If the lactam carbonyl is located in the inner ring of cis-quinolizidine, it is exceptionally resistant to the action of the indicated reagents.

A different behavior of the trans- and cis-quinolizidine rings in the molecule of alkaloids of the sparteine series toward the action of oxidizing agents has been shown. Upon oxidation of alkaloids with a cis-quinolizidine system by potassium ferricyanide and potassium permanganate in acetone solution, a lactam group is formed very readily. Alkaloids with a trans-quinolizidine system are not oxidized under these conditions.

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