THIN-LAYER CHROMATOGRAPHIC ANALYSIS OF THE PRODUCTS OF THE HYDROGENATION OF ANABASINE, AMMODENDRINE, AND ISOAMMODENDRINE

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On reducing l-anabasine (I) under various conditions, Orekhov [1] obtained a mixture of hydro derivatives of anabasine from which he isolated l-α,β-bipiperidyl. Later a number of workers [2-5] obtained this base preparatively and determined the conditions for its TLC [6].

When ammodendrine (II) was reduced and then subjected to alkaline hydrolysis, d, l-α, β-bipiperidyl was obtained [7]. Under similar conditions, isoammodendrine (III) forms d-α,β-bipiperidyl [8].

In hexahydroanabasine and hydrogenated N-acetylanabasine (IV) new asymmetric carbon atoms appear, which justifies the assumption of the formation of several stereoisomers from each of them. Furthermore, the bipiperidyls described in the literature [7, 8] are apparently not individual products of the reduction of saponified II and III. In view of this, in order to establish the uniformity and identify the products of the reduction of I, II, II, and IV by comparison with authentic samples, we have used thin-layer chromatography in a nonfixed layer of alumina.

Anabasine was hydrogenated with sodium in isoamyl alcohol and also in the presence of Adams catalyst in hydrochloric acid solution. Compounds II, III, and IV were reduced only catalytically.

TABLE 1. R_f Values of the Products of the Hydrogenation of α-Anabasine, N-Acetylanabasine, Ammodendrine, and Isoammodendrine

Compound	R_f in solvent systems	
	$CHCl_3$ (sat. with NH_3) – C_6H_6 – CH_3OH (15:18:1.5)	$CHCH_3$ (sat. with NH_3) – C_6H_6 – CH_3OH (35:5:1.5)
1-Anabasine	0,60	0,72
Ammodendrine	0,58	0,77
Dihydroammodendrine	0,44	0,66
Isoammodendrine	0,59	0,78
Dihydroisoammodendrine		
No. 1'	0,40	—
No. 2'	0,44	—
No. 3'	0,46	—
No. 4'	0,48	—
α,β-Bipiperidyl		
No. 1	0,10	0,45
No. 2	0,14	0,37
No. 3	0,18	0,34
No. 4	0,22	0,26
N-Acetylanabasine	0,62	0,80
Hexahydro-N-acetylanabasine		
No. 1''	0,25	0,53
No. 2''	0,28	0,58
No. 3''	0,30	0,61
No. 4''	0,36	0,65
Decomposition products		
No. 5	0,62	—
No. 6	0,66	—

By using highly polar systems of solvents saturated with ammonia and long plates, substances with R_f values of 0.26, 0.34, 0.37, and 0.45 were detected in the products of the hydrogenation of I.

The l-α,β-bipiperidyl obtained as described by Orekhov [1] was still nonuniform after repeated recrystallization and chromatographic purification through the hydrochloride. Two spots appeared with R_f values of two stereoisomers (Nos 2 and 3) of the four hexahydro derivatives of anabasine (Table 1).

A comparative chromatogram of the combined bases from the hydrogenated I and II shows that the saponified dihydroammodendrine (V) consists of two epimers the R_f values of which correspond to the R_f values of stereoisomers Nos. 2 and 3. In the case of V, only one spot was found.

Four substances were found in the products of the hydrogenation of III: Nos. 1' 2', 3' and 4'. The R_f values of substances No. 2 and V coincide. When the total bases from hydrogenated III were subjected to alkaline hydrolysis, substances Nos. 1, 2, 3, and 4

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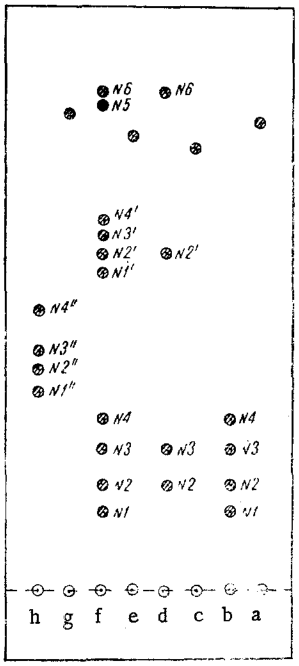

Fig. 1. Results of thin-layer chromatography: a) *l*-anabasine; b) hydrogenated *l*-anabasine; c) ammodendrine; d) hydrogenated ammodendrine; e) isoammodendrine; f) hydrogenated isoammodendrine; g) N-acetylanabasine; h) hydrogenated N-acetylanabasine.

were found, the R_f values of which correspond to those of hydrogenated I.

The combined bases from hydrogenated N-acetylanabasine contain substances Nos. 1", 2", 3", and 4", the R_f values of which do not correspond to those of V and the hydrogenated III.

Almost no products of the decomposition of anabasine were detected while for II they amounted to about 15-20% and for III to 80-85%. The R_f values of these substances (Nos. 5 and 6) are greater than those of the initial II and III.

It did not prove possible to separate the stereoisomeric α,β-bipiperidyls found and to isolate them in the pure state by preparative chromatography because of the smallness of differences in their R_f values.

EXPERIMENTAL

l-Anabasine was obtained from technical anabasine sulfate via the N-acetyl derivative, bp 186-188° C/2 mm; n_D^{20} 1.5516 [9]. The base was redistilled in vacuum, bp 125° C/5 mm; n_D^{20} 1.5441.

Ammodendrine (from the collection of the Institute of Chemistry, Academy of Sciences of the Moldavian SSR) was the base with mp 73-74°C (from aqueous ether). Isoammodendrine (a sample given to us by Professor Kh. A. Aslanov) gave a hydriodide with mp 218-219°C.

The hydrogenation of *l*-anabasine was carried out by the action of sodium on a solution of the base in isoamyl alcohol [10]. The hydrogenation products (bp 104-117°C/2 mm; 52 g) were dissolved in 350 ml of absolute ether, and a current of CO_2 precipitated a mixture of all the hexahydro derivatives in the form of carbonates, from which the combined bases were obtained by well-known methods, after which they were crystallized from a small amount of ether, mp 48-61°C. TLC showed the presence of substances Nos. 1, 2, 3, and 4. The hydrochlorides of the combined bases were precipitated from absolute ethanol and recrystallized from 95% C_2H_5OH, mp 312-314°C, base with mp 69-70°C (from ether) in which TLC showed the presence of two substances – Nos. 2 and 3.

The catalytic hydrogenation of anabasine (0.5 g), N-acetylanabasine (0.5 g), ammodendrine (0.2 g), and isoammodendrine (0.16 g) was performed with hydrogen in 0.1 N HCl solution over platinum oxide. Compounds I and IV formed mixtures of bases consisting of Nos. 1, 2, 3, and 4 and Nos. 1", 2", 3", and 4", respectively; II formed dihydroammodendrine (2'); and III formed Nos. 1', 2', 3', and 4' (bp 138-150°C/2 mm), i.e., dihydroisoammodendrine (VI). When V and VI were subjected to alkaline hydrolysis for 24 h, a mixture of substances Nos. 1 and 2 and Nos. 1, 2, 3, and 4, respectively, contaminated with the decomposition products Nos. 5 and 6, were obtained.

Thin-Layer Chromatography. The products of the hydrogenation of I, II, III, and IV and also the total bases after the hydrolysis of V and VI were dissolved in ether and chromatographed in a thin nonfixed layer of alumina (activity grade II). The solvents used were carefully purified and dehydrated methanol, benzene, and chloroform saturated with ammonia. The dimensions of the plates were 27 × 9 cm and the thickness of the layer of sorbent 0.5 mm. The substances investigated were deposited on the layer of Al_2O_3 in amounts of 10-15 μg. These spots were revealed with iodine vapor.

SUMMARY

It has been shown by TLC on a nonfixed layer of Al_2O_3 that the hydrogenation of *l*-anabasine forms four stereoisomers and that of N-acetylanabasine three substances, and the conditions for their chromatography and their R_f values have been determined.

The α,β-bipiperidyl described previously is actually a mixture of two stereoisomers to which, according to their R_f values, saponified dihydroammodendrine and dihydroisoammodendrine correspond.

The product of the reduction of ammodendrine is identical in R_f value with one of the four products from dihydroisoammodendrine. Their hydrolysis leads to the formation of the corresponding stereoisomers of α,β-bipiperidyl.

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