THE SEPARATION OF THE ALKALOIDS OF Anabasis aphylla

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UDC 547.944/661.2

A new method for the separate isolation of the alkaloids of A. aphylla based on the extract of the high-boiling fraction (HBF) of the bases with chloroform from anabasine sulfate and also on the separation of a mixture of anabasine and lupinine by nitrosation, has been developed previously [1].

In the extract of the high-boiling bases with chloroform, a small amount (10-15%) of anabasine also passes into the solvent, which makes an additional separation of this mixture by vacuum distillation necessary.

By using various conditions of extraction, we have attempted to achieve the complete isolation of the high-boiling bases free from anabasine.

Before extraction, the anabasine sulfate was diluted with water and was also additionally acidified to a definite pH of the medium. When the HBF of the alkaloids was extracted without dilution, the extraction time amounted to 3.5-4 h, and ~ 10% of anabasine passed into the chloroform extract in addition to the high-boiling alkaloids. When the anabasine sulfate was diluted with water (4 : 3), the time of extraction fell to 1 h, and the amount of anabasine in the chloroform extract fell correspondingly – to 2% (Table 1). We measured the pH values of the solutions of the individual alkaloids under the same conditions with the aid of a pH-meter (pH 340) (Table 2).

Knowing that the alkaloids studied differ considerably in basicity, we attempted to extract them at various pH values of the medium. When a dilute solution (4 : 3) of anabasine sulfate was acidified to pH 4, the anabasine and the lupinine did not pass into the solvent, and it was mainly the weakest bases – aphylline and anabasamine – that were extracted (Table 3). The optimum pH of the medium for the extraction of the high-boiling alkaloids is 5.

We have developed a method for converting the high-boiling alkaloids (aphylline, aphyllidine) into pachycarpine by catalytic hydrogenation [2]. The presence of low-boiling alkaloids among the high-boiling

TABLE 1. Extraction of Anabasine Sulfate with Chloroform as a Function of the Dilution

Expt. No.	Anabasine sulfate taken, g	Dilution with water	Amount of HBF		
			chloroform extract, ml	after distillation of the chloroform: total amount of HBF, g	after distillation of the chloroform: amount of anabasine in the HBF, %
1	2000	Without dilution	4215	136,30	10,40
2	2000	4 : 1	4195	132,47	7,53
3	2000	4 : 2	4100	125,35	3,33
4	2000	4 : 3*	4100	124,30	1,83

*On 1 : 1 dilution, the time of extraction increases.

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Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 468-472, July-August, 1974. Original article submitted February 23, 1973.

TABLE 2. pH Values of the Alkaloids of A. aphylla (H_2O–CH_3OH, 1:1)

Alkaloid	Concentration, M	Temperature, °C	pH
Anabasine	0,01	27	10,26
Lupinine	0,01	27	10,83
Aphylline	0,01	28	9,76
Aphyllidine	0,01	28	9,56
Anabasamine	0,01	26	9,12

bases considerably complicates the isolation of the pachycarpine. In the present paper we also describe a method for eliminating contaminating anabasine and lupinine from the HBF. The method is based on the formation of the carbonates of the strong bases – in our case, anabasine and lupinine. The residual weak bases (aphylline, aphyllidine, etc.) can be separated in the free state by extracting with xylene or ether the aqueous solution saturated with carbon monoxide (Table 4).

Where necessary, anabasamine can easily be obtained from a mixture of the three components by hydrolysis with 25% sulfuric acid. The lactam-containing alkaloids – aphylline and aphyllidine – are converted into the corresponding amino acids, and the anabasamine, after the mixture has been made alkaline and extracted with chloroform, is isolated in the individual state.

EXPERIMENTAL

Thin-layer chromatography was performed on a nonfixed layer of alumina (activity grade II). The solvent system for anabasine and lupinine was acetone–water (100:8) and that for aphylline, aphyllidine, and anabasamine was chloroform–ether (35:50).

The amounts of the individual alkaloids in the fractions were determined by thin-layer chromatography and (after the spots had been revealed in iodine vapor) the elution of the spots with 0.1 N hydrochloric acid followed by titration with 0.01 M of silicotungstic acid. For paper chromatography we used type "M" ["slow"] paper from the Volodarskii Leningrad Mill.

Extraction of the Alkaloids of the HBF. The high-boiling fraction was extracted under various conditions of the pH of the medium and dilution with water. Consequently, we give only typical experiments.

A. Technical anabasine sulfate containing 31.5% of anabasine (1000 g) was extracted with chloroform (5-7 times) until the aphylline and aphyllidine had been extracted completely (according to thin-layer chromatography). The consumption of chloroform was 3100 ml. After drying (Na_2SO_4) and distillation of the solvent, the residue (58.10 g) contained 7.8% of anabasine, 53.2% of aphylline, 21.6% of aphyllidine, 12.80% of anabasamine, and a very small amount of lupinine.

B. To 2000 g of anabasine sulfate was added 1500 ml of water, and the mixture was stirred until it was homogeneous. Then it was extracted with chloroform (6 × 700 ml). After drying (Na_2SO_4) and distillation of the solvent, the residue (124.2 g) contained 1.83% of anabasine.

C. A total of 9000 g of anabasine sulfate with pH 5.8 was separated into nine 1000-g samples, each was brought to a volume of 1750 ml (dilution with water in a ratio of 4:3), the pH values were adjusted to predetermined levels (see Table 3) by the addition of sulfuric acid, and each was extracted separately with chloroform until HBF was absent (according to chromatography). The chloroform was distilled off and the amounts of the individual components were determined chromatographically* (see Table 3).

Separation of the Mixture of Alkaloids with the Aid of Carbon Dioxide. Typical experiment. With heating (70-80°C), 124.2 g of the mixture of alkaloids was diluted with 250 ml of water and, after cooling, 63 g of solid carbon dioxide (dry ice) was added, and the mixture was shaken for 15 min. Then it was extracted with m-xylene until alkaloids were absent (test with Dragendorff's reagent), which required six treatments with 200 ml of solvent each. After drying (Na_2SO_4) and the distillation of the solvent, the residue (97.8 g) consisted of a mixture of aphylline (64.35%), aphyllidine (20.10%), and anabasamine (8.36%). The aqueous solution was made strongly alkaline and extracted with m-xylene until alkaloids were absent (5 × 150 ml). After distillation of the solvent, the residue (18.6 g) contained 1.80% of anabasine and traces of lupinine (according to thin-layer chromatography).

Isolation of Anabasamine. To 97.8 g of the HBF was added 225 ml of 25% sulfuric acid, and the mixture was heated on the water bath at 95-100°C for 12 h. The solution was made alkaline and was extracted with chloroform. After drying (Na_2SO_4) and the distillation of the solvent, the residue (7.9 g) was recrystallized from petroleum ether, giving anabasamine with mp 67-68°C.

* The mixture contains neutral bases which do not appear on chromatography and are not considered in determining the amounts of alkaloids.

TABLE 3. Extraction of the High-Boiling Alkaloids at Various pH Values from Technical Anabasine Sulfate

Expt. No.	Anabasine sulfate, diluted 4:3, taken, g	pH of the anabasine sulfate taken	Chloroform extract, ml	Total amount, g	Amounts of alkaloids, % (after distillation of the chloroform			
					anabasine	aphylline	aphyllidine	anabasamine
1	1750	3,00	2230	22,10	—	—	55,10	35,00
2	1750	3,40	2100	28,70	—	15,0	48,30	31,50
3	1750	3,80	2100	36,10	—	20,15	42,00	28,70
4	1750	4,20	2090	46,20	1,12	35,40	36,20	20,10
5	1750	4,60	2090	48,18	1,62	43,10	31,10	17,60
6	1750	5,00	2070	51,16	2,10	49,65	26,80	16,40
7	1750	5,40	2050	56,30	5,50	50,25	25,20	15,10
8	1750	5,60	2050	56,80	6,80	53,70	22,50	13,20
9	1750	5,80	2050	58,10	7,80	53,20	21,60	12,80

TABLE 4. Separation of a Mixture of Alkaloids by means of Carbon Dioxide

Expt. No.	HBF* taken, g	Amount of alkaloids after separation (on the HBF), %				
		aqueous fraction		xylene fraction		
		anabasine	lupinine	aphylline	aphyllidine	anabasamine
1	25	6,12	Traces	60,35	15,20	6,10
2	30	10,60	2,50	56,0	15,10	7,15
3	50	9,50	2,16	58,50	15,30	7,25
4	50	9,56	2,20	58,70	15,28	7,36
5	100	11,40	3,36	50,50	20,40	6,60
6	100	11,36	3,30	51,10	22,0	6,20
7	124,2†	1,80	Traces	64,35	20,10	8,36

* Starting materials from various batches.
† Obtained by 4:3 dilution (see Table 1).

From the aqueous solution after neutralization (pH 6-7) and cyclization in an autoclave at 210-220°C for 5 h, a mixture of aphylline and aphyllidine (56.8 g) was isolated.

SUMMARY

1. The optimum conditions for the extraction of the high-boiling alkaloids from technical anabasine sulfate by dilution with water and at various pH values of the medium have been established.

2. A method for removing anabasine and lupinine from a mixture of the high-boiling alkaloids of Anabasis aphylla has been developed which is based on the formation of the carbonates of the strong bases.

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