A NEW METHOD FOR ISOLATING THE ALKALOIDS OF Anabasis aphylla

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UDC 547.944/661.2

Anabasine sulfate from the central Asian plant A. aphylla [1] is a good insecticide [2] which is being manufactured in the Chimkent factory for pharmaceutical chemicals.

In anabasine sulfate, only anabasine, the amount of which is 70-75% of the total bases, possesses insecticidal properties, and the accompanying alkaloids [3, 4] (10-15% of lupinine, 5-10% of aphylline, 5-10% of aphyllidine, 4-5% of anabasamine, and ~1% of oxoaphylline and hydroxyaphyllidine) are "ballast."

We have shown [5] that the high-boiling fraction of the alkaloids of Anabasis aphylla (aphylline, aphyllidine) can be reduced in good yield to pachycarpine, which is obtained industrially from Sophora pachycarpa. Another alkaloid – lupinine – may also have independent value, since some preparations made from it are anesthetic substances [6]. Aphylline hydrochloride is distinguished by a long-acting anesthetic effect [7]. We have previously developed a method for isolating it from the high-boiling fraction of the anabasis alkaloids and from the crystalline wastes from the production of anabasine [8]. Furthermore, free anabasine may be used as a preparation which stimulates the growth and development of the cotton plant [9].

On the basis of the above facts, we propose the separate isolation and use of all the alkaloids of technical anabasine.

Several methods exist for the laboratory separation of the mixture of alkaloids [1]. They are all laborious and are based on the isolation of the combined alkaloids from anabasine sulfate, the fractionation of the alkaloids in vacuum into low-boiling (anabasine, lupinine) and high-boiling (aphylline, aphyllidine, anabasamine), and the subsequent separation of the low-boiling fraction. These methods cannot be used under industrial conditions in view of their technological difficulties and economic disadvantages. An exception is the sulfuric acid method of separation [10], which permits the alkaloids to be extracted directly from the anabasine sulfate. However, this method is associated with the use of a large amount of conc. sulfuric acid at a high temperature (90-100°C) and with the subsequent treatment of the mixture with concentrated alkali. This leads not only to difficulties in the choice of the material of construction of the apparatus but also to the formation of a large amount of sodium sulfate residue which, naturally, complicates the technological process. We have improved and modified some production processes and have developed a unitary scheme for the isolation of the individual alkaloids from anabasine sulfate using the high-boiling fraction to obtain aphylline and pachycarpine. The proposed scheme can be recommended for industrial use.

In direct extraction of anabasine sulfate with chloroform, the aphylline, aphyllidine, and a small amount of anabasine pass into the chloroform extract. The bulk of the anabasine and lupinine remain in the anabasine sulfate. Then, by nitrosation of an acid aqueous solution it is possible to isolate lupinine and anabasine from the anabasine sulfate in the form of the nitroso derivatives [11].

We have studied the hydrolysis of nitrosoanabasine to anabasine under various conditions. The optimum conditions are the use of 18% hydrochloric acid at 98-100°C. With sulfuric acid (20-25%) hydrolysis takes place comparatively slowly (on heating for 10 h, only 20-25% of the nitrosoanabasine is saponified).

V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 324-328, May-June, 1972. Original article submitted March 31, 1971.

TABLE 1. Results of the Sulfation of a Kerosine Extract

Amount of 40% H_2SO_4, ml	T, °C	Time of sulfation, h	Anabasine sulfate			High-boiling fraction	
			amt., g	anabasine, %	free acid, %	g	%
25	70–80	4,5	68	34,5	0,56	2,1	3,1
25	50–60	5,3	72,2	32,4	0,49	5,4	7,5
25	40–50	7,4	70,5	28,0	0,51	4,4	6,2

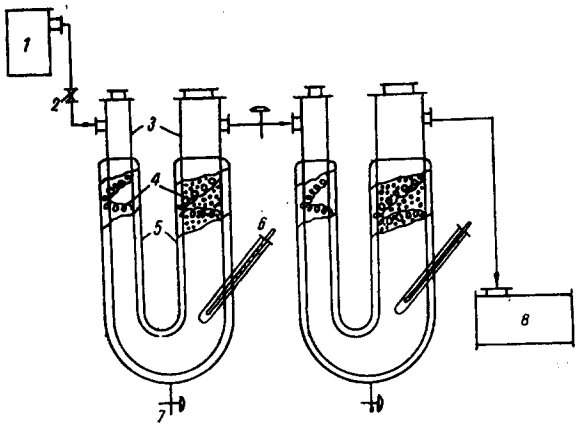

Fig. 1. Apparatus for the extraction of alkaloids from a strong kerosine extract with sulfuric acid: 1) vessel for the strong kerosine extract; 2) cock; 3) column; 4) electric heater; 5) asbestos insulation; 6) thermometer; 7) cock for run-off; 8) receiver for the spent kerosine extract.

In the production of anabasine sulfate, during the sulfation of the mixture of alkaloids with 40% sulfuric acid (70-80°C) a considerable amount of aphylline and aphyllidine is hydrolyzed, forming the corresponding amino acids. The optimum conditions for retaining the maximum amount of high-boiling alkaloids in the anabasine sulfate (Fig. 1) were achieved by sulfating the kerosine extract with 40% sulfuric acid at 50-60°C (Table 1).

The promising schemes for the isolation of the alkaloids of anabasine and for obtaining pachycarpine from a mixture of high-boiling bases that have been developed permit the profitability of the production of anabasine to be raised considerably, with the simultaneous elimination of the necessity for a special factory for the production of pachycarpine from Sophora pachycarpa.

EXPERIMENTAL

Sulfation of a Kerosine Extract. A factory kerosine extract was passed through a battery of glass columns (see Fig. 1) filled with small fragments of glass, fitted with an electric heater, and containing 40% sulfuric acid, at the rate of about 2 liters/h at 50-60°C.

When the anabasine sulfate had reached a neutral reaction, the first column was removed from the battery and the passage of the kerosine extract was continued with the following column, and so on. The anabasine sulfate obtained was analyzed for its content of anabasine, high-boiling fractions, and free sulfuric acid. The amount of anabasine was determined by the standard method [1], that of the high-boiling fraction by weighing, and that of the free sulfuric acid by titration (see Table 1).

Extraction of the High-Boiling Alkaloids. Technical anabasine sulfate (500 g) was repeatedly extracted with chloroform (200-ml portions) until the high-boiling alkaloids had been eliminated completely [thin-layer chromatography on alumina of activity grade II in the acetone–water (100 : 8) system]. All the extracts were combined (1.4 liter), the chloroform was distilled off, and the residue (23.2 g), containing the aphylline, aphyllidine, anabasamine, and a small amount of anabasine, was distilled in vacuum at 2 mm Hg. The following fractions were obtained: I) 6.0 g of anabasine* (120-130°C); II) 13.2 g of aphylline and aphyllidine (160-170°C); and III) 3.1 g of anabasamine (170-180°C).

Nitrosation. A. After extraction with chloroform, 400 g of technical anabasine sulfate (35% of anabasine) was dissolved in 500 ml of 15% sulfuric acid. With cooling and continuous stirring, 90 g (1.5 moles with respect to the anabasine) of sodium nitrite in 321 ml of water was added dropwise to the solution. Stirring was continued for 3 h. Then the reaction mixture was left to the following day, after which the product was treated with 153 ml of 40% caustic soda solution and exhaustively extracted with 1.4 liters of chloroform. After the chloroform had been distilled off, 157.4 g (96%) of a nitrosoanabasine residue with R_f 0.65 [paper chromatography, butan-1-ol–water–hydrochloric acid (100 : 27 : 13)] was obtained. The

*The anabasine fraction can be returned to the anabasine sulfate material.

neutral aqueous solution was made alkaline (to phenolphthalein) with 122 ml of 40% NaOH and was extracted with 1300 ml of chloroform until the reaction for alkaloids (Dragendorff's reagent) was negative. The chloroform was distilled off and the residue – 12.4 g (3.1%) of technical lupinine – had mp 67-68°C after recrystallization from petroleum ether.

B. After the chloroform extraction of the high-boiling alkaloids (12.5 g) and nitrosation under the conditions of the preceding experiment, 200 g of anabasine sulfate (33.2% of anabasine) was made alkaline (pH 10-11) with 40% caustic soda and exhaustively extracted with chloroform. The chloroform was distilled off giving a residue of 90.2 g of nitrosoanabasine and lupinine.

Distillation at 3 mm gave fraction I, consisting of 13.4 g of lupinine (130-140°C), and fraction II, consisting of 57.3 g of nitrosoanabasine (170-180°C).

Hydrolysis of Nitrosoanabasine. A solution of 150 g of nitrosoanabasine in 828 ml of 18% hydrochloric acid (1 : 7 molar) was heated at 98-100°C for 8 h, by which time the nitrosoanabasine had been completely hydrolyzed. Then the solution was made alkaline (to phenolphthalein) with 350 ml of 40% caustic soda and was extracted with 3 liters of chloroform; the chloroform was evaporated off and the residue – 23.2 g (97%) of free anabasine – after distillation (120-130°C at 2 mm) gave in the mass spectrum a molecular peak with m/e 162.

Hydrogenation of the High-Boiling Alkaloids. A solution of 100 g of the mixture of bases in 500 ml of dioxane was treated with 100 g of copper–chromium catalyst ($CuCrO_4$). The mixture was stirred in an autoclave under a pressure of 120 atm of hydrogen at 150-160°C for 14 h. After reduction, the catalyst was filtered off and the solvent was removed in vacuum at 10-20 mm. The residue (92.2 g) was distilled at 4 mm.

This gave fraction I consisting of 58.2 g (61.2%) of pachycarpine with $[\alpha]_D$ + 16.2° (methanol) (150-170°C), and fraction II* consisting of 28.1 g (28.1%) of a mixture of aphylline and aphyllidine (180-190°C).

A saturated aqueous solution of ammonium iodide was added to the pachycarpine. White crystals of pachycarpine monohydriodide precipitated instantaneously. After two recrystallizations from ethanol, the substance had mp 233-234°C. A mixture of the monohydriodides of synthetic and natural pachycarpines showed no depression of the melting point.

SUMMARY

1. A new method for the separation and isolation of the alkaloids of Anabasis aphylla from technical anabasine sulfate has been developed.

2. The possibility has been shown of the simultaneous production of anabasine sulfate, pachycarpine monohydriodide, and anabasine, and also of free lupinine, from anabasis.

LITERATURE CITED

1. A. S. Sadykov, The Chemistry of the Alkaloids of Anabasis aphylla [in Russian], Tashkent (1956).
2. S. S. Stankov, Useful Wild Plants of the USSR [in Russian], Moscow (1951), p. 129.
3. A. P. Orekhov, Zh. Obshch. Khim., 7 2048 (1937).
4. Kh. A. Aslanov, S. Z. Mukhamedzhanov, and A. S. Sadykov, Nauchnye Tr. TashGU – Khimiya Rastitel'nykh Veshchestv, 1966, No. 2, 286.
5. Kh. A. Aslanov, A. S. Sadykov, A. I. Ishbaev, and N. D. Abdullaev, Nauchnye Tr. TashGU – Khimiya Rastitel'nykh Veshchestv, 1966, No. 2, 67.
6. L. G. Merkulov, Farmakol., 7, 37 (1938).
7. I. É. Akopov and V. A. Konovalova, Farmakologiya i Toksikologiya, 1949, No. 1; 1950, No. 4.
8. A. I. Ishbaev, A. S. Sadykov, and Kh. A. Aslanov, Zh. Obshch. Khim., 33, 687 (1963).
9. S. A. Askarova, A. S. Sadykov, O. S. Otroshchenko, K. D. Dzhumashev, and R. Zhaksinbaeva, Proceedings of an All-Union Symposium on the Fight against Cotton Wilt [in Russian], Tashkent (1964).
10. O. S. Otroshchenko, A. S. Sadykov, and Kh. A. Arbarov, Zh. Obshch. Khim., 29, 2441 (1959).
11. A. P. Orekhov and G. P. Men'shikov, Byull. NIKhFI, 1931, No. 1.

* Fraction II may be added to a new portion of high-boiling alkaloids.