At the present time, the \( \beta \)-picoline fraction, consisting of pyridine bases that boil in the range 138-146\(^\circ\), is used for the production of nicotinic and isonicotinic acids [1]. This fraction represents a mixture of bases close in properties, which substantially hinders the isolation of the individual components.

We have developed a method of analyzing the \( \beta \)-picoline fraction with the aid of gas-liquid chromatography, permitting a step-by-step control in the production of nicotinic and isonicotinic acid (see scheme).

The \( \beta \)-picoline fraction was analyzed on a two-meter column of stainless steel with an inner diameter of 4 mm, filled with the solid carrier spherochrome-1* with particle size 0.15-0.3 mm, with 12\% polyethylene glycol sebacate (PEGS). The velocity of the helium carrier gas was 140 ml/min, temperature of the system 115\(^\circ\), of the evaporator 250\(^\circ\), and the detector was a katharometer. Figure 1 presents a chromatogram of one of the industrial samples of the \( \beta \)-picoline fraction. On the basis of the data that we obtained, the following average composition (in \%) was found for the investigated \( \beta \)-picoline fraction: impurities - 1.2 (1), pyridine - 0.6 (2), \( \alpha \)-picoline - 17.5 (3), 2,6-lutidine - 24 (4), \( \beta \)-picoline - 30 (5), \( \gamma \)-picoline - 25.1 (6), 2,4-lutidine - 1.6 (7). The change in the composition of the \( \beta \)-picoline fraction during

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*The carrier was previously manufactured under the trade name TND-TS-M.

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Fig. 1. Gas-liquid chromatography of the \(\beta\)-picoline fraction. Here and in Figs. 2-3, the notations are given in the text.

The distillation in the temperature range 138-146° was also studied by gas-liquid chromatography. As can be seen from Fig. 2, when the temperature of distillation is increased, the content of pyridine (1, in Fig. 2) and \(\alpha\)-picoline (2) decreases, and the content of \(\beta\)- (5) and \(\gamma\)- (4) picolines increases. The fraction 2,6-lutidine (3) changes negligibly. In the last fraction, collected at temperatures above 146°, up to 8% 2,5- and 2,4-lutidines were detected.

In preparative organic chemistry, the reaction of formulation is used for the removal of \(\gamma\)-picoline from the \(\beta\)-picoline fraction. The mono-, di-, and tri-\(\gamma\)-methylolpicolines formed in this case are removed. After removal of \(\gamma\)-picoline, the pyridine bases remaining were analyzed by gas-liquid chromatography. The following substances were identified (in %): formaldehyde - 4, water - 28, 2,6-lutidine - 21, \(\alpha\)-, \(\beta\)-, and \(\gamma\)-picolines - 12.8, 30.4, and 3.8, respectively.

The use of the method of gas-liquid chromatography for the analysis of pyridine bases makes it possible to do without an approximate analysis by paper chromatography and permits a calculation of the required amount of copper sulfate and sulfuric acid at the following stage of isolation of the complex salt of \(\beta\)-picoline with copper sulfate. The isolated aqueous solution of \(\beta\)-picoline was analyzed by gas-liquid chromatography.

For several industrial samples we obtained the following average composition of the aqueous solution of \(\beta\)-picoline (in %): \(\beta\)-picoline - 34.5, \(\alpha\)-picoline - 0.4, 2,6-lutidine - 1.1, and water - 63. For a qualitative determination of impurities of \(\alpha\)-picoline and 2,6-lutidine, we used the method of normalization (reduction to 100%) [2].

To obtain nicotinic acid, \(\beta\)-picoline is oxidized with potassium permanganate. The unreacted \(\beta\)-picoline is distilled off and added to the following operation of oxidation. The following composition of the distilled aqueous solution of \(\beta\)-picoline was obtained: about 10% \(\beta\)-picoline and 90% water; after salting out with sodium hydroxide, the product contained 1.9% \(\alpha\)-picoline, 3.1% 2,6-lutidine, and 95% \(\beta\)-picoline.

The mother liquors obtained after the isolation of nicotinic acid were neutralized with sodium carbonate, evaporated, and separated from the potassium chloride.

We verified the possibility of the coprecipitation of pyridinecarboxylic acids with inorganic salts, for which the inorganic mass was treated with ethanol and sulfuric acid. The ethyl esters of pyridinecarboxylic acids were isolated by the well known method and analyzed by the method of gas-liquid chromatography that we developed (12% PEGS on spherochrome-1 at a temperature of the system 180-200°, column length 2 m). The following percent content of pyridinecarboxylic acids in the potassium chloride precipitate was established (Fig. 3a): isonicotinic acid - 0.3 (1), nicotinic acid - 2.5 (2), \(\alpha\)-picolinic acid - 0.3 (3), and 2,6-lutidinic acid - 3.

The proposed method of esterification of pyridinecarboxylic acids opens up the way for supplementary extraction of pyridinecarboxylic acids from the inorganic salts isolated. According to our data, 50 tons of inorganic salts contain up to 1.5 tons of nicotinic acid.

The nicotinic and isonicotinic acids produced by the oxidation of \(\beta\)-picoline and \(\gamma\)-methylolpicolines were tested for the possible presence of other pyridinecarboxylic acids. For this purpose, nicotinic and isonicotinic acids were preliminarily converted to the ethyl esters and studied by gas-liquid chromatography. Pharmacopoeia samples showed the absence of impurities in the form of other pyridinecarboxylic acids (Fig. 3b).

The mixture separated from \(\beta\)-picoline and brought into aqueous solution possesses the following composition (in %): 2,6-lutidine - 42, \(\alpha\)-picoline - 21.8, \(\beta\)-picoline - 6.2, water - 30. Then 2,6-lutidine