CATALYTIC ALKYLATION OF PYRIDINE AND ITS HOMOLOGS. PREPARATION OF 3,5-LUTIDINE AND 3-ISOPROPYLPYRIDINE

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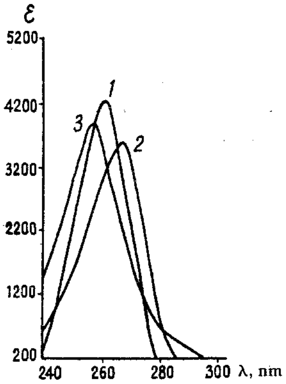
When the catalytic alkylation of pyridine was carried out with methanol and dimethyl ether under high-pressure conditions the main product was 3, 5-lutidine. In the alkylation of 3-picoline with methanol, the main product was 3-isopropylpyridine.

Recently, 3,5-dialkylpyridines, especially 3,5-dimethylpyridine, have found use as intermediates in the production of synthetic resins, dyes, and pharmaceutical preparations [1].



UV spectra in 1% sulfuric acid: 1) 3-methylpyridine; 2) 3,5-dimethylpyridine; 3) 3-isopropylpyridine.

Synthetically, 3,5-lutidine is obtained by the condensation of propionaldehyde with formaldehyde and ammonia [2], by the condensation of α-methylacrolein with ammonia [3], and by the catalytic reduction of the corresponding halogen derivatives of pyridine [4, 5]. The preparation of alkylpyridines directly from pyridine by catalytic alkylation with ethanol is limited to the work of Cullinane [6]. He obtained a complex mixture of 3- and 4-picolines, 2,6-lutidine, and other pyridine derivatives in low yield.

In contrast to this work, we have studied the catalytic alkylation of pyridine and 3-picoline with methanol and of pyridine with dimethyl ether at high pressures. The reactions were carried out both in an autoclave and in a continuous system. In this process we used industrial active alumina and narrow-pored alumino-silicate as catalysts. It was found that the reaction of pyridine with methanol (taken in a molar ratio of 1 : 6) in an autoclave with the catalysts mentioned gave mainly 3,5-lutidine. The optimum yield of the latter (30.8%) was found with a three-hour time of contact of the starting materials with the aluminosilicate catalyst at 400° C. No appreciable difference in the effectiveness of the catalysts was found. In this reaction only a very small amount of 3-picoline was formed.

The use of dimethyl ether as alkylating agent in the presence of active alumina under the same conditions led to a small increase in the yield of 3,5-lutidine (35.1% calculated on the initial pyridine). In the alkylation of 3-picoline with methanol over aluminosilicate under the same conditions, 3-isopropylpyridine and 3,5-lutidine were formed in yields of 7.5 and 2.0%, respectively.

We have also carried out the alkylation of pyridine on the catalysts mentioned with dimethyl ether in a continuous system at a space velocity of pyridine of 0.078 hr^{-1}. In this case, the yield of the 3,5-lutidine fraction was only 6% of the initial pyridine. The small yield of 3,5-lutidine in this case is probably explained by the considerably lower pressure (10 atm) than in the autoclave reaction (300–350 atm).

EXPERIMENTAL

The alkylation of pyridine with methanol was carried out in an autoclave of type AV-1 with a capacity of 1 *l*. A mixture of 59 g of dry freshly-distilled pyridine, 142 g of absolute methanol, and 260 ml of calcined catalyst was charged into the autoclave. Then it was heated to the predetermined temperature (400° C) over 2 hr, and the time of contact of the reactants with the catalysts was calculated from the moment when this temperature was reached. The discharged catalyzate was dried with granulated potassium hydroxide for a day and was then subjected to two fractional distillations.

The following fractions were isolated and identified: 1) 140–150° C, 0.6 g, n_D^{20} 1.4988 – 3-picoline. The UV spectrum of the product regenerated from the picrate: λ_{max} 262 nm [7] (see figure). **Picrate**, mp 150° C. Found, %: C 44.50; H 3.10; N 17.30, mol. wt. 324. Calculated for $C_6H_7N \cdot C_6H_3N_3O_7$, %: C 44.10; H 3.13; N. 17.39, mol. wt. 322.

2) 165–175° C, 19.8 g, n_D^{20} 1.4967 – 3, 5-lutidine. The UV spectrum of the product regenerated from the picrate: λ_{max} 267.5 nm. **Picrate**, mp 237.5° C (from water). Found, %: C 46.51; H 3.59; N 16.66. Calculated for $C_7H_9N \cdot C_6H_3N_3O_7$, %: C 46.43; H 3.57; N 16.66.

3) 176–185° C, 4.9 g, n_D^{20} 1.4998 – also identified as 3, 5-lutidine. UV spectrum of the product regenerated from the picrate: λ_{max} 267.5 nm. **Picrate**, mp 236.6° C. Found, %: C 46.21; H 3.64; N 16.41.

The alkylation of pyridine with dimethyl ether was carried out in the following way: the autoclave was initially charged with 110 g of pyridine and 260 ml of catalyst and then, in the cold, 128 g of the liquified ether was added. The remainder of the process was carried out as described above. Distillation of the product at 730 mm gave two fractions: 167–175° C, 117 g, and 175–180° C, 31 g. Both fractions were identified as 3, 5-lutidine. UV spectrum of the product regenerated from the picrate: λ_{max} 267.5 nm. **Picrate**, mp 237–238° C. Found, %: N 16.43; mol. wt. 335.

The alkylation of 3-picoline was carried out by the method described above. The autoclave was charged with 71.0 g of dehydrated 3-picoline, 142.0 g of absolute methanol, and 260 ml of aluminosilicate.

Two distillations of the alkylate yielded the following fractions: 1) 48–52° C (5 mm), 1.5 g – 3, 5-lutidine. UV spectrum of the product regenerated from the picrate: λ_{max} 267.5 nm. **Picrate**, mp 238° C. Found, %: C 46.39; H 3.43; N 16.71.

2) 53–58° C (5 mm), 7 g, n_D^{20} 1.4918 – 3-isopropylpyridine. UV spectrum of the product regenerated from the picrate: λ_{max} 258 nm. **Picrate**, mp 138° C (from water). Found, %: C 48.10; H 3.81; N 15.98, mol. wt. 348. Calculated for $C_8H_{11}N \cdot C_6H_3N_3O_7$, %: C 48.02; H 4.03; N 15.99, mol. wt. 350.2.

The alkylation of pyridine with dimethyl ether was carried out in a continuous flow apparatus [8]. A cylinder with the liquified ether was attached to the apparatus, and this created a pressure in the system of about 10 atm. The reservoir was charged with 60 g of the initial pyridine. The pyridine was passed over 130 ml of the catalyst heated to 400° C in a current of compressed dimethyl ether. At the end of the process, the alkylate was distilled and two fractions were isolated: 166–175° C (n_D^{20} 1.4997) and 175–180° C (n_D^{20} 1.4983) at 715 nm, with yields of 3.5 and 1.5 g, respectively. Both fractions were identified as 3, 5-lutidine. **Picrate**, mp 235–236° C. Found, %: N 16.71; mol wt. 334.2.

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