CATALYTIC ALKYLATION OF PYRIDINE AND ITS HOMOLOGS

II.* ALKYLATION OF 2-PICOLINE WITH METHANOL IN THE PRESENCE OF HYDROGEN CHLORIDE

V. N. Gudz', S. A. Trifonova, and A. N. Shpagina

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In the reaction of 2-picoline with methanol in the presence of hydrogen chloride, alkylation proceeds primarily at the side methyl group to form 2-ethyl- and 2-isopropylpyridines, together with small amounts of 3-picoline and 2,3- and 2,6-lutidines.

In connection with a study of the alkylation of pyridine on acid catalysts [1,2], it seemed of interest to investigate the reaction of picolines with methanol in the presence of hydrogen chloride. 2- And 4-picolines are capable of undergoing alkylation in the side chain by means of organometallic compounds. There is only one indication [4] of the alkylation of 2-picoline with methanol in the presence of aluminum oxide. In this case, 2-ethylpyridine is formed in 45% yield along with 2-isopropylpyridine in 5% yield. We studied the alkylation of 2-picoline with methanol in the presence of hydrogen chloride, applied on silica gel. The reaction was carried out in both an autoclave and in a flow system. In the autoclave variant, 2-picoline is alkylated primarily in the side chain to form 2-ethyl- (60%) and 2-isopropylpyridines (5.7%). In addition, ring alkylation to form 2,6- (1.7%), 2,3- (2.2%), and 2,5-lutidines (1.8%), isomerization of 2-picoline with migration of a methyl group to the 3 position (0.9%), and dealkylation of 2-picoline to pyridine (1.7%) occur under the process conditions.

In the flow variant, the formation of 2-ethylpyridine in 7.4% yield was observed during alkylation of 2-picoline, and 5.2% of the 2-picoline underwent dealkylation, while 2% of the 2-picoline was isomerized. Traces of 2,6-, 2,5-, and 2,3-lutidines were detected in the mixture of alkylated products.

Thus increased pressure of the reaction mixture is an important factor in alkylation. On the other hand, however, dealkylation and isomerization of 2-picoline proceed more vigorously at normal pressure.

EXPERIMENTAL

The alkylation of pyridine was carried out in a type AB-1 autoclave at 350°C and 200-210 atm. A 72-g sample of freshly distilled anhydrous 2-picoline and 140 g of absolute methanol, together with the catalyst (0.1 mole), uniformly applied on silica gel, were placed in the autoclave. The contact time of the reaction mixture with the catalyst was reckoned from the point at which a fixed temperature was reached. The catalyzate was acidified with 20% hydrochloric acid, and the neutral products were removed by steam distillation. The residue was treated with 30% sodium hydroxide solution until it was alkaline, and the pyridine bases were removed by steam distillation. The bases were salted out with potassium carbonate, dried with potassium hydroxide, and fractionally distilled. The fractions selected were analyzed with an LKhM-7A gas-liquid chromatograph with a flame-ionization detector. A flexible four-meter column with an inner diameter of 6 mm was used for the separation; 2 m of this column was filled with INZ-600 brick, to which 20% triethanolamine + 2% potassium hydroxide had been applied; the other 2 m of the column was filled with Cellite-545, to which 20% polyethylene glycol (with a molecular weight of 1000) + 3.6% potassium hydroxide had been applied. The columns were thermostatted at 150°, and the argon flow rate was 30 ml/

*See [1] for communication I.

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TABLE 1. Results of Fractionation and Characteristics of the Isolated Alkylpyridines

bp, °C	Amt., g	Components	Comp. %	bp, °C	Amt., g	Components	Comp., %
114—140	23,4	Pyridine	3,2	160—180	14,8	2-Picoline	7,1
		2-Picoline	41,6			2,6-Lutidine[c]	1,0
		2,6-Lutidine[a]	2,0			2-Ethylpyridine	74,8
		2-Ethylpyridine[b]	48,5			2-Isopropyl-pyridine	9,6
		2,5-Lutidine	4,7			2,3-Lutidine	7,5
140—160	48,5	Pyridine[c]	0,6				
		2-Picoline	24,0	180—200	8,6	3-Picoline[c]	traces
		2,6-Lutidine[a]	2,2			2-Picoline	4,3
		2-Ethylpyridine	65,0			2-Ethylpyridine	60,0
		2,5-Lutidine[c]	0,9			3-Picoline	4,6
		2-Isopropyl-pyridine	7,3			2-Isopropyl-pyridine[d]	19,1
		2,3-Lutidine[a]	traces			2,3-Lutidine	12,0

[a]Identified by addition of a reference substance to the investigated sample.
[b]The picrate had mp 109°. Found: N 16.6%. $C_7H_9N \cdot C_6H_3N_3O_7$. Calculated: N 16.7%.
[c]Identified from the retention time.
[d]The picrate had mp 119°. Found: N 16.1%. $C_8H_{11}N \cdot C_6H_3N_3O_7$. Calculated: N 16.0%.

min. The peaks were identified by selection of microquantities of the individual components issuing from the flow meter with subsequent investigation of them by UV spectroscopy with an SF-4A spectrophotometer, from the exit times of the peaks, and by the addition of a reference substance fraction to the investigated sample. The results of the fractionation and identification of the pyridine bases are presented in Table 1.

The alkylation of pyridine in the flow variant was accomplished in an apparatus of the flow system in [5] at a 2-picoline space velocity of 0.074 h^{-1}, 450°, and atmospheric pressure of the vapors of the reacting substances. A mixture of 40 g of 2-picoline and 70 g of methanol was passed over 180 cm^3 of heated (to 400°) silica gel impregnated with 0.1 mole of hydrogen chloride. At the end of the process, the catalyzate was worked up by the method indicated above and fractionated. The following fractions were isolated: the first fraction (33.8 g) with bp 127-135° consisted of 5.2% pyridine, 83.3% 2-picoline, 9.3% 2-ethylpyridine, and 2.2% 3-picoline (the 3-picoline was identified by addition of a standard to the investigated sample followed by chromatography); the second fraction (1.4 g) with bp 135-140° consisted of 1.1% pyridine, 68.7% 2-picoline, 4.6% 2,6-lutidine, 18.5% 2-ethylpyridine, 2.3% 3-picoline, 1.9% 2,5-lutidine, and 2.9% 2,3-lutidine. The pyridine, 3-picoline, and 2,5- and 2,3-lutidines were identified by addition of standards to the investigated samples with subsequent chromatography of the mixtures.

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