THE REACTION OF PENTACHLOROPYRIDINE WITH AROMATIC AMINES

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UDC 547.822.5.7

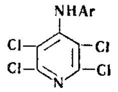
The reaction of pentachloropyridine with aromatic amines in dimethylformamide in the presence of sodium carbonate leads to 4-arylaminotetrachloropyridines. The product of the reaction of pentachloropyridine with aniline in pyridine is 4-amino-2,3,5,6-tetrachloropyridine.

Continuing investigations begun previously on the chemistry of pentachloropyridine [1] (I), we have studied the reaction of I with aromatic amines. According to the literature [2-4], the reaction between I and nucleophilic reagents takes place in position 4 of the pyridine ring as a rule. However, the reaction between I and aliphatic amines at a comparatively low temperature takes place predominantly in position 2 of the pyridine ring [1,5,6].

In the reaction of I with aromatic amines, it was found that only amines with well-marked nucleophilic properties, such as p-toluidine and p-anisidine, react readily under the conditions that are the optimum for aliphatic amines. It was impossible to perform this reaction with aniline and other aromatic amines containing electron-accepting groups in the benzene ring. Attempts to obtain arylaminotetrachloropyridines from aromatic amines of low basicity and I by other methods of condensing aromatic amines with heterocyclic compounds containing active halogens that have been described in the literature, namely heating I with an excess of the amine under pressure in the presence of copper [7], heating the reactants without a solvent in the presence of potassium carbonate, and carrying out the reaction in aqueous acetone solution in the presence of mineral acids [9], did not give satisfactory results either.

It was possible to achieve satisfactory results only by carrying out the reaction in dimethylformamide in the presence of sodium carbonate. The arylaminotetrachloropyridines obtained (Table 1) form low-melting crystalline substances readily soluble in the usual organic solvents.

TABLE 1

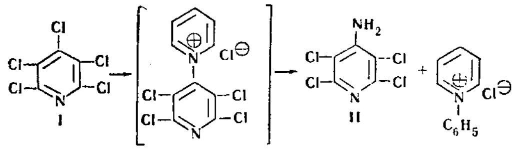


Ar	mp, °C	Crystallization solvent	Empirical formula	Found, %		Calc., %		Yield, %
				Cl	N	Cl	N	
m-Br-C_6H_4	180—181	Heptane	$C_{11}H_5BrCl_4N_2$	36,76	7,25	36,71	7,23	60
m-Cl-C_6H_4	158—159	Heptane	$C_{11}H_5Cl_5N_2$	51,85	8,15	51,82	8,17	50
p-Cl-C_6H_4	148—149	Heptane	$C_{11}H_5Cl_5N_2$	52,16	8,24	51,82	8,17	36
p-O_2N-C_6H_4	277—278	Ethanol	$C_{11}H_5Cl_4N_3O_2$	40,66	12,06	40,22	11,89	40
C_6H_5	103—104*	Heptane	$C_{11}H_6Cl_4N_2$	45,85	9,07	46,10	9,06	65
p-H_3C-C_6H_4	125—126	Ethanol	$C_{12}H_8Cl_4N_2$	44,40	8,62	44,09	8,69	45
p-CH_3O-C_6H_4	115—116	Ethanol	$C_{12}H_8Cl_4N_2O$	42,52	8,24	42,01	8,28	38

*bp 162-165°C (1 mm).

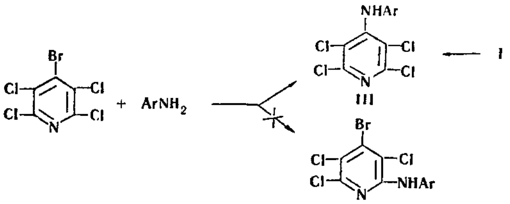
Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 7, pp. 963-965, July, 1970. Original article submitted April 22, 1969.

In an attempt to obtain anilinotetrachloropyridine from I and aniline in the presence of pyridine, it was found that I reacts with pyridine in a similar manner to chlorodinitrobenzene with the formation of 2,3,5,6-tetrachloropyridin-4-ylpyridinium chloride, which is cleaved by the aniline, giving 4-amino-2,3,5,6-tetrachloropyridine (II) and N-phenylpyridinium chloride, which was identified in the form of its perchlorate.



The structure of II was shown by its independent synthesis directly from I and ammonia [2].

To determine the structure of the products of the condensation of I with aromatic amines, independent syntheses of arylaminotetrachloropyridines starting from 4-bromo-2,3,5,6-tetrachloropyridine were carried out.



In this case it was possible to expect the formation of two different products: 4-arylamino-tetrachloropyridines (III) and 2-arylamino-4-bromo-3,5,6-trichloropyridines. However, the reaction took place with the formation of III (absence of a bromine atom from the reaction products). Similar products are obtained by the condensation of I with aromatic amines. Thus, the reaction of I with aromatic amines leads to the splitting out of the halogen atom in position 4 and to the production of 4-arylamino-2,3,5,6-tetrachloropyridines.

On the basis of the experimental material obtained on the condensation of I with amines, a definite relationship is revealed between the basicity of the amine and the direction of its attack on the pyridine ring. Amines in which the pH is less than 7 usually attack position 4 in I, and those in which the pH is greater than 7 attack position 2.

EXPERIMENTAL

4-Amino-2,3,5,6-tetrachloropyridine (II). A mixture of 2.5 g (0.01 mole) of I, 0.93 g (0.01 mole) of aniline, 5 ml of pyridine, and 15 ml of dimethylformamide was heated in the oil bath with stirring at 150°C for 10 min, after which the temperature was lowered to 100°C and kept at this level for another 3 h. After cooling, the contents of the flask were poured into water slightly acidified with hydrochloric acid, and the precipitate of II was filtered off and washed with water. Yield 1.6 g (70%), mp 212-215°C (from heptane). Found %: Cl 61.15; N 12.16. $C_5H_2Cl_4N_2$. Calculated %: Cl 61.20; N 12.06. After the water and dimethylformamide had been eliminated from the filtrate from II in vacuum, a viscous oil of N-phenylpyridinium chloride remained, from which the perchlorate was obtained. Yield 2.1 g (82%). mp 220-222°C (from water) (according to the literature [11], mp 221°C). Found %: Cl 14.09; N 5.56. $C_{11}H_{10}ClNO_4$. Calculated %: Cl 13.89; N 5.47.

2,3,5,6-Tetrachloro-4-(p-methoxyphenylamino)pyridine. A solution of 5 g (0.02 mole) of I in 50 ml of ethanol was treated with 7.4 g (0.06 mole) of p-anisidine and was heated with vigorous stirring at 60-70°C for 4 h. The solvent was distilled off in vacuum and the residue was treated with 100 ml of 2% HCl. The precipitate was filtered off and crystallized from aqueous ethanol (Table 1).

2,3,5,6-Tetrachloro-4-(p-tolylamino)pyridine was obtained similarly.

4-Anilino-2,3,5,6-tetrachloropyridine. a. A solution of 5 g (0.02 mole) of I in 50 ml of absolute dimethylformamide was treated with 2 g (0.021 mole) of freshly distilled aniline and 3 g (0.026 mole) of Na_2CO_3, and the mixture was heated at 150-160°C with vigorous stirring for 3 h. Then it was cooled, part of the dimethyl formamide was distilled off in vacuum, and the residue was poured into 150 ml of 2% HCl.

The oil that separated out was extracted twice with ether, the extract was dried with sodium sulfate, the ether was driven off, and the residue was distilled in vacuum. On the addition of petroleum ether, the distilled oil crystallized instantaneously.

b. A solution of 3 g (0.01 mole) of 4-bromo-2,3,5,6-tetrachloropyridine [10] in 50 ml of absolute dimethylformamide was treated with 1 g (0.01 mole) of freshly distilled aniline and 1.5 g (0.013 mole) of Na_2CO_3 and the mixture was heated at 160°C with vigorous stirring for 2 h. All the remainder of the process was similar to method a. Yield 2.2 g (70%). mp 101-102°C (from heptane). Found %: Cl 46.69; N 9.05. $C_{11}H_6Cl_4N_2$. Calculated %: Cl 46.10; N 9.09.

2,3,5,6-Tetrachloro-4-(p-tolylamino)pyridine was also obtained by method b. Yield 75%. mp 126°C (from heptane). Found %: Cl 43.58. $C_{12}H_8Cl_4N_2$. Calculated %: Cl 44.09. The reactions of I with nitro-, chloro-, and bromoanilines were carried out by method a (Table 1).

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