REACTIONS OF PENTACHLOROPYRIDINE WITH ORGANOMAGNESIUM COMPOUNDS

Ya. N. Ivashchenko, S. D. Moshchitskii, and A. K. Eliseeva

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4-Alkyltetrachloropyridines were obtained by the interaction of pentachloropyridine with halogenated magnesium alkyl compounds in an ether–tetrahydrofuran solution.

Continuing the investigation of the action of nucleophilic reagents on pentachloropyridine [1], we studied the interaction of pentachloropyridine with halogenated magnesium alkyl compounds.

Unlike 2- and 3-monohalogenated substituted pyridines, which under usual conditions do not form Grignard compounds [2–4] and do not react with halogenated magnesium alkyl compounds [5], pentachloropyridine I easily reacts with magnesium [6] and with halogenated magnesium alkyl compounds to form the corresponding 4-derivatives of 2, 3, 5, 6-tetrachloropyridine. The attack of halogenated magnesium alkyl compounds on the fourth position of pentachloropyridine agrees with the view as to the greatest reaction capacity of this position towards nucleophilic reagents [7–12].

A peculiarity of the reaction of pentachloropyridine (I) with halogenated magnesium alkyl compounds is that it proceeds satisfactorily only in the presence of tetrahydrofuran (THF), employed as a solvent for I. The reaction does not proceed when diethyl ether alone is employed both to prepare the Grignard reagent and to dissolve I. The best results as to yields and purity of the products were obtained when the Grignard reagents were prepared in ether, and tetrahydrofuran or a mixture of equal volumes of tetrahydrofuran and ether were employed as solvent for I.

Methyl iodide, ethyl bromide, n-propyl and n-butyl and benzyl chloride were used as starting materials to prepare Grignard reagents. It was not feasible to obtain 4-methyl-2, 3, 5, 6-tetrachlorpyridine (II) from methyl magnesium bromide and I. Compound II was obtained only after replacing methyl bromide by methyl iodide (yield 25%). From the products of this reaction, and with about 35% yield, 4, 4'-bipyridyl-2, 2', 3, 3', 5, 5', 6, 6'-octachloro(III) was also separated. Compound III was probably obtained through 2, 3, 5, 6-tetrachloropyridyl-4-magnesium chloride, which may be easily formed by the presence of an excess of magnesium in the reaction medium [6]. Compound II was also synthesized through 2, 3, 5, 6-tetrachloropyridylmalonic ester and 2, 3, 5, 6-tetrachloropyridyl-4-acetic acid (IV) [9].

The well known tetrachloroisonicotinic acid (V) was obtained by the oxidation of II with potassium permanganate [6, 13, 14].

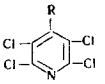
EXPERIMENTAL

4-Methyl-2, 3, 5, 6-tetrachloropyridine (II). A) A solution of 17.5 g (0.07 mole) of I in 100 ml of a mixture of absolute tetrahydrofuran and ether was added drop by drop to an ethereal solution of methyl magnesium iodide (from 2.4 g Mg and 14 g methyl iodide) under continuous stirring at such speed that the ether was kept boiling uniformly and smoothly. After the pentachloropyridine was added, the reaction mixture was heated for 2 hr at 50–60° C. The ether and the tetrahydrofuran were then distilled off. The residue was carefully treated first with water and then with chloroform. The emulsion formed was broken down by filtration through a Büchner funnel. The chloroform solution was dried over $CaCl_2$ and the solvent was distilled off. The residue was dissolved in ethanol, out of which III precipitated, mp 247–248° C (ex ethanol), yield 35%. Found, %: Cl 65.22; N 6.22. Calculated for $C_{10}Cl_8N_2$, %: Cl 65.74; N 6.48. After elimination of the ethanol, II was distilled under vacuum.

B) 2.75 g (0.01 mole) of compound IV was gradually heated on an oil bath to 200° C, and kept at this temperature for 1 hr, mp. 90° C, yield 95%. Found, %: Cl 61.29. Calculated for $C_6H_3Cl_4N$, %: Cl 61.47. No depression of the melting point was observed in a mixed sample of compound II obtained by methods A and B.

The 4-alkyltetrachloropyridines presented in the table were obtained in a similar way: addition of a solution of I in tetrahydrofuran to a solution of magnesium alkyl bromide in ether.

4-Alkyl-2, 3, 5, 6-tetrachloropyridines



R	Bp, °C (pressure, in mm)	Mp, °C, (crystallizing solvent)	Molecular formula	Found, %		Calculated, %		Yield, %
				Cl	N	Cl	N	
CH_3	90 (0.02)	89—90 (ethanol + water)	$C_6H_3Cl_4N$	61.99	6.42	61.47	6.06	25
C_2H_5	93 (0.02)	67—68 (acetic acid + water)	$C_7H_5Cl_4N$	58.02	5.74	57.95	5.70	85
n-C_3H_7	94—95 (0.02)	—	$C_8H_7Cl_4N$	54.26	5.59	54.82	5.40	62
n-C_4H_9	100 (0.07)	—	$C_9H_9Cl_4N$	51.92	5.24	52.01	5.12	68
$C_6H_5CH_2$	165 (0.15)	105—107 (ethanol)	$C_{12}H_7Cl_4N$	46.22	4.53	46.25	4.56	42

2, 3, 5, 6-Tetrachloroisonicotinic acid (V). To 1.15 g (0.005 mole) of II in 30 ml water at 80–90° C was gradually added 1.5 g of $KMnO_4$ in the course of 30 hr. The excess of $KMnO_4$ was destroyed by adding 5 ml of methanol. The hot solution was freed from MnO_2 by filtration, and evaporated to 1/3 its volume. The solution was acidified with dil (1 : 1) hydrochloric acid and left in a cold place overnight. 0.2 g (15%) of acid V was obtained, mp 220–222° C (ex water). Found, %: Cl 54.36; N 5.38. Calculated for $C_6HCl_4NO_2$, %: Cl 54.40; N 5.36.

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Institute of Organic Chemistry AS UkrSSR, Kiev