REACTIONS OF 2-AMINOPYRIDINES WITH PHOSPHORUS PENTACHLORIDE

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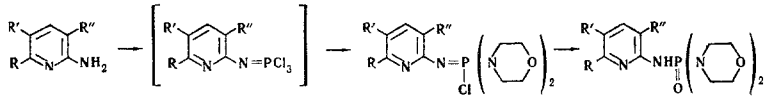
The reaction of 2-aminopyridines with PCl_5 proceeds with the formation of 2-trichlorophosphazopyridines, which when treated with morpholine are converted to 2-dimorpholidochlorophosphazopyridines. By heating these last products with 96% ethanol, dimorpholido pyridyl-2-amidophosphoric acids are obtained.

It had been previously established [1, 2] that 2- and 4-aminopyrimidines react with PCl_5 to form monomeric trichlorophosphazopyridines, similar to amides of carboxylic acids and sulfanilamides [3]. This reaction had not been studied within the series of 2-aminopyridines. It could be expected that, due to a lowering of the electronic density on the exocyclic nitrogen atom in 2-aminopyridines [4, 5], these might react with PCl_5 in the same way as 2- and 4-aminopyrimidines and aminotriazines [6], i.e., with the formation of monomeric trichlorophosphazopyridines. These last compounds are interesting as starting substances for the synthesis of various organophosphorous compounds.



I a–g II a–g III a–g IV a–g

a R=R″=H, R′=Cl; b R=R″=H, R′=Br; c R=R″=H, R′=J; d R=R″=H, R′=NO_2; e R=H, R′=R″=Cl; f R=R′=R″=H; g R=CH_3, R′=Br, R″=H

The HCl liberated in the reaction of 2-aminopyridines (I) with PCl_5 was collected and back-titrated. When weak bases (I, R-halogens, NO_2) were introduced into the reaction, 2 equivalents of HCl were collected, but when strong bases were introduced (R=H) –1 equivalent was collected and the hydrochloride of trichlorophosphazopyridine was formed.

Trichlorophosphazopyridines (II) proved very unstable under ordinary conditions, and therefore were not isolated; but their formation was demonstrated by their conversion to the more stable dimorpholidochlorophosphazopyridines (III). Conversion of III to dimorpholidopyridyl-2-amidophosphoric acids (IV) was achieved by boiling in ethanol. Compound IVc was obtained from IIIc, without separation, by boiling in ethanol.

EXPERIMENTAL

2-Dimorpholidochlorophosphazo-5-chloropyridine (IIIa). A suspension of 1.5 g (11.7 mM) of 2-amino-5-chloropyridine and 2.43 g (11.7 mM) of PCl_5 in 30 ml benzene was boiled for 2 hr under stirring and in a current of nitrogen. To the reaction mixture, consisting of a solution of 2-trichlorophosphazo-5-chloropyridine in benzene, and after cooling to 10–15° C, a solution of 4.07 g (46.8 mM) of morpholine in 20 ml of benzene was added, and stirring was continued for 3 hr at 20° C. The morpholine hydrochloride was filtered off, washed with benzene, the mother liquors were united, the benzene distilled off under vacuum, the residual oil was dissolved in 100 ml of dry ether, stirred up with charcoal, filtered off, the ether distilled off, and the residual oil crystallized by rubbing. In a similar way compounds (IIIb–IIIe) were obtained (see Table 1). These dissolved easily in organic solvents. Compound III was slowly hydrolyzed when exposed to the air.

2-Dimorpholidochlorophosphazopyridine (IIIf). A suspension of 1.5 g (15.9 mM) of 2-aminopyridine and 3.32 g (15.9 mM) of PCl_5 in 40 ml benzene was boiled in a current of nitrogen and stirred for 2 hr. The reaction mixture was cooled, the precipitate filtered off, washed with ether, yielding 3.91 g of the hydrochloride of 2-trichlorophosphazopyridine. This was then suspended in 100 ml ether, cooled to 10–15° C, and 6.4 g (5 equiv) of morpholine in 20 ml ether was added while stirring. Stirring was continued for 30 min at 15° C, 3 hr at 20° C, and then the mixture was allowed to stand until the following day. The morpholine hydrochloride was filtered off, washed with ether, the mother liquors were united, the ether partly evaporated, and the residue passed through an Al_2O_3 column, which was then eluted with ether. The eluate was evaporated, and the residual oil was crystallized by rubbing.

Table 1. 2-Dimorpholidochlorophosphazopyridines (III)

Compound	Mp °C (ex ether)	Molecular formula	Found, %					Calculated, %					Yield, %
			C	H	Cl (Br)	N	P	C	H	Cl (Br)	N	P	
IIIa	77—79	$C_{13}H_{19}Cl_2N_4O_2P$	42.63	5.27	19.68	15.70	8.39	42.75	5.24	19.42	15.34	8.48	82
IIIb	101—102	$C_{13}H_{19}BrClN_4O_2P$	37.82	4.67	28.10**	13.83	7.82	38.11	4.68	28.18*	13.68	7.58	92.3
IIIc	121—122	$C_{13}H_{19}ClIN_4O_2P$	34.09	4.14	—	12.42	6.48	34.19	4.19	—	12.27	6.78	82.8
IIId	107—108	$C_{13}H_{19}ClN_5O_4P$	41.91	5.19	9.44	18.38	8.08	41.55	5.10	9.44	18.64	8.06	87.5
IIIe	117—119	$C_{13}H_{18}Cl_3N_4O_2P$	38.74	4.67	26.49	14.26	7.80	39.07	4.54	26.62	14.02	7.75	92
IIIf	77—78	$C_{13}H_{20}ClN_4O_2P$	47.12	5.91	10.42	17.40	9.45	47.20	6.10	10.72	16.94	9.37	54

*From ether.
**Total chlorine and bromine.

Table 2. Dimorpholides of pyridyl-2-amidophosphoric acids (IV).

Compounds	Mp. °C (solvent for crystallization)	Molecular formula	Found, %					Calculated, %					Yield, %
			C	H	Cl (Br) (I)	N	P	C	H	Cl (Br) (I)	N	P	
IVa	147—148 (ethyl acetate)	$C_{13}H_{20}ClN_4O_3P$	45.28	5.80	10.03	16.07	8.72	45.03	5.81	10.23	16.16	8.93	86.4
IVb	177.5—178.5 (ethyl acetate)	$C_{13}H_{20}BrN_4O_3P$	40.31	5.10	20.43	14.31	7.70	39.91	5.15	20.43	14.32	7.92	76.8
IVc	198—199 (methanol)	$C_{13}H_{20}IN_4O_2P$	35.71	4.55	28.21	12.77	6.78	35.63	4.60	28.96	12.79	7.07	93.7
IVd	121—122 (ethyl acetate)	$C_{13}H_{20}N_5O_5P$	43.80	5.74	—	19.85	8.93	43.70	5.64	—	19.60	8.67	68.8
IVe	147.5—148 (ethyl acetate)	$C_{13}H_{19}Cl_2N_4O_3P$	41.27	5.24	18.75	14.90	7.70	40.96	5.02	18.60	14.70	8.13	94.5
IVf	156—157 (ethyl acetate)	$C_{13}H_{21}N_4O_3P$	49.55	6.78	—	17.59	10.15	49.99	6.78	—	17.94	9.92	89
IVg	174.5—175 (benzene)	$C_{14}H_{22}BrN_4O_3P$	41.73	5.48	19.75	13.58	7.74	41.49	5.47	19.72	13.83	7.64	80.5

Dimorpholid of 5-chloropyridyl-2-amidophosphoric acid (IVa). Five grams of compound IIIa was suspended in 50 ml ethanol, boiled for 45 min, then cooled and neutralized with an ethanolic solution of triethylamine or with an ethanolic solution of KOH. The solvent was distilled off under vacuum, and the residue was boiled with 50 ml benzene*. Compound IVa was obtained after the benzene was distilled off. In a similar way were obtained compounds IVb–IVg (Table 2), very soluble in chloroform and ethanol, while IVa, IVd–IVg were easily soluble in water.

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*In the case of compound IVc, the residue after distillation of the solvent was washed with water and then crystallized.