REACTIONS OF 5-AMINOPYRIMIDINES WITH PHOSPHORUS PENTACHLORIDE

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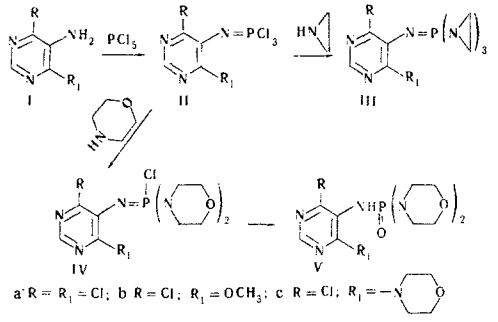
5-Amino-4,6-dichloro-, 5-amino-4-chloro-6-methoxy-, and 5-amino-4-chloro-6-morpholinopyrimidines react with PCl_5 to form monomeric 5-(trichlorophosphoranyleneamino)pyrimidines.

We have previously found that unsubstituted 2- and 4-aminopyrimidines and the corresponding compounds with substituents in the ring react with PCl_5 in a similar manner to amides with the formation of monomeric 2- and 4-(trichlorophosphoranylideneamino)pyrimidines [1, 2].

It appeared of interest to study the reaction of PCl_5 with 5-aminopyrimidines in view of the fact that the latter have properties resembling those of the weak aromatic amines which, as is well known, with a few exceptions, on reaction with PCl_5 form dimeric trichlorophosphoranylideneaminoarenes [3]. A study of this reaction was begun with 5-aminopyrimidines containing substituents in positions 4 and 6.



a R = R_1 = Cl; b R = Cl; R_1 = OCH_3; c R = Cl; R_1 = –N(O)

The phosphorylation of I was carried out in benzene at 70° C. In all cases there was a rapid (~1.5 hr) evolution of two equivalents of hydrogen chloride. The 5-(trichlorophosphoranylideneamino)pyrimidines (II) so formed consist of crystalline substances with low melting points readily soluble in inert organic solvents. It was found by molecular weight determinations that they are monomeric. The 5-(trichlorophosphoranylideneamino)pyrimidines rapidly hydrolyze on standing in the air. In water they hydrolyze to the initial 5-aminopyrimidines **I**. Like the 2- and 4-(trichlorophosphoranylideneamino)pyrimidines and the monomeric trichlorophosphoranylideneamino compounds of other series [4–6], the 5-(trichlorophosphoranylideneamino)pyrimidines readily react with amines under ordinary conditions. With ethyleneimine they form triethyleneiminophosphoranylideneaminopyrimidines (III) and with morpholine chlorodimorpholinophosphoranylideneaminopyrimidines (IV). Compounds **IV** readily hydrolyze in the air and in boiling 96% ethanol to 5-(dimorpholinophosphonylamino)pyrimidines (V). In the reaction of **Va** with morpholine, one of the chlorine atoms is readily replaced by morpholine under the usual conditions.

EXPERIMENTAL

4,6-Dichloro-5-(trichlorophosphoranylideneamino)pyrimidine (IIa). A suspension of 2 g (0.0122 mole) of 5-amino-4,6-dichloropyrimidine and 2.54 g (0.0122 mole) of phosphorus pentachloride in 40 ml of benzene was heated at 70° C and stirred in a current of nitrogen for 1 hr 30 min. The resulting solution was stirred with carbon and filtered, and the benzene was distilled off in vacuum to give 3.21 g (88%) of **IIa** with mp 38–42° C. Found, %: Cl_{ion} 33.55%; mol. wt. 283.0. Calculated for $C_4HCl_5N_3P$, %: Cl_{ion} 35.54; mol. wt. 299.3.

4-Chloro-5-(trichlorophosphoranylideneamino)-6-methoxypyrimidine (IIb) was obtained similarly. Yield 89.5%, mp 80–85° C; Found, %: Cl_{ion} 34.6; mol. wt. 282.0. Calculated for $C_5H_4Cl_4N_3OP$, %: Cl_{ion} 35.07; mol. wt. 294.9.

4,6-Dichloro-5-[tri(ethyleneimino)phosphoranylideneamino]pyrimidine (IIIa). A suspension of 2 g (0.0122 mole) of 5-amino-4,6-dichloropyrimidine and 2.54 g (0.0122 mole) of PCl_5 in 10 ml of benzene was heated in a current of nitrogen at 70° C and stirred for 1 hr 30 min. The solution was cooled to 8–10° C and at this temperature, with stirring, a solution of 1.68 g (0.0366 mole) of ethyleneimine and 3.7 g (0.0366 mole) of triethyleneimine in 30 ml of benzene was added to it. After this, the reaction mixture was stirred at 20° C for 2 hr, the triethyleneimine hydrochloride was filtered off and washed with benzene, the mother liquors were combined, the benzene was distilled off in vacuum, and the residue was washed with petroleum ether to give 3.14 g (80.8%) of **IIIa**, mp 86.5–88° C (from ether). Found, %: C 37.92; H 4.29; Cl 21.49; N 26.33; P 9.64. Calculated for $C_{10}H_{13}Cl_2N_6P$, %: C 37.63; H 4.11; Cl 22.22; N 26.33; P 9.7.

The following were obtained similarly: **4-chloro-5-[tri(ethyleneimino)phosphoranylideneamino]-6-methoxypyrimidine (IIIb)** with a yield of 68.2%, mp 72–73.5° C (from ether). Found, %: C 42.15; H 5.03; Cl 11.10; N 26.68; P 9.44. Calculated for $C_{11}H_{16}ClN_6OP$, %: C 41.98; H 5.12; Cl 11.27; N 26.70; P 9.84; and **4-chloro-5-[tri(ethyleneimino)phosphoranylideneamino]-6-morpholinopyrimidine (IIIc)** with a yield of 87%, mp 146–146.5° C (from benzene). Found, %: C 45.63; H 5.78; Cl 9.46; N 26.16; P 8.50. Calculated for $C_{14}H_{21}ClN_7OP$, %: C 45.47; H 5.72; Cl 9.59; N 26.51; P 8.38.

4,6-Dichloro-5-(chlorodimorpholinophosphoranylideneamino)-pyrimidine (IVa). With stirring and cooling (6–8° C), 3.19 g (0.0366 mole) of morpholine in 10 ml of benzene was added in a current of nitrogen to a solution of 2.74 g (0.00914 mole) of **IIa** in 40 ml of benzene. The reaction mixture was stirred with cooling for 30 min and at 20° C for 2 hr and was left to the following day. The morpholine hydrochloride was filtered off and washed with benzene, the mother liquors were combined, the benzene was distilled off in vacuum, and the residual oil was crystallized from a small amount of petroleum ether. Yield 3.54 g (96.7%), mp 126–127.5° C (from ether). Found, %: H 35.72; H 4.22; Cl_{tot} 26.63; Cl_{ion} 8.6; N 17.32; P 7.60. Calculated for $C_{12}H_{17}Cl_3N_5O_2P$, %: C 35.97; H 4.28; Cl_{tot} 26.55; Cl_{ion} 8.85; N 17.48; P 7.73.

4-Chloro-5-(chlorodimorpholinophosphoranylideneamino)-6-morpholinopyrimidine (IVc) was obtained similarly. Yield 77.6%, mp 136–138° C (from benzene). Found, %: C 43.00; H 5.60; Cl 15.33; N 18.47; P 6.89. Calculated for $C_{16}H_{25}Cl_2N_6O_3P$, %: C 42.58; H 5.58; Cl 15.71; N 18.62; P 6.86.

4,6-Dichloro-5-(dimorpholinophosphonylamino)pyrimidine (Va). A solution of 2.17 g of **IVa** in 15 ml of 96% ethanol was boiled for 15 min and then the reaction mixture was neutralized with a solution of triethylamine in benzene. The solvent was distilled off in vacuum, the residue was boiled with ethyl acetate (3 × 70 ml) and filtered off, and the ethyl acetate was distilled in vacuum to give 1.61 g (77.6%)

of **Va**. After crystallization from ethyl acetate, mp 184.5–186° C. Found, %: C 37.75; H 4.77; Cl 18.54; N 18.36; P 8.04. Calculated for $C_{12}H_{18}Cl_2N_5O_3P$, %: C 37.71; H 4.75; Cl 18.55; N 18.33; P 8.10.

4-Chloro-5-(dimorpholinophosphonylamino)-6-methoxy-pyrimidine (Vb) was obtained similarly; yield 62.9%, mp. 213.5–214° C (from ethyl acetate). Found, %: C 41.15; H 5.45; Cl 9.34; N 18.32; P 7.9. Calculated for $C_{13}H_{21}ClN_5O_4P$, %: C 41.33; H 5.60; Cl 9.39; N 18.54; P 8.20.

4-Chloro-5-(dimorpholinophosphonylamino)-6-morpholinopyrimidine (Vc). a) By the preceding method, yield 75.4%, mp 194–196° C (from methanol). Found, %: C 44.23; H 5.97; Cl 8.18; N 19.49; P 7.20. Calculated for $C_{16}H_{26}ClN_6O_4P$, %: C 44.39; H 6.05; Cl 8.19; N 19.42; P 7.16.

b) A solution of 0.4 g (0.00105 mole) of **Va** and 0.18 g (0.0021 mole) of morpholine in 5 ml of methanol was left at 20° C for a day. The solvent was evaporated off to half bulk, and the precipitate was filtered off to give 0.24 g (54%) of **Vc**. A mixture with the sample obtained by method (a) gave no depression of the melting point.

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