# DICHLORANHYDRIDES OF PYRIMIDYL-4-AMIDOPHOSPHORIC ACIDS

N. V. Sazonov and A. A. Kropacheva

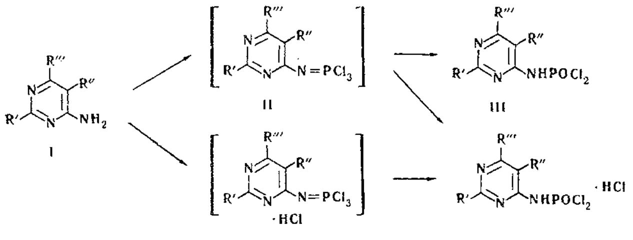
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 1, pp. 97–99, 1970

UDC 547.853.7

4-Trichlorophosphazopyrimidines or their hydrochlorides were obtained by the reaction between 4-aminopyrimidines and phosphorus pentachloride. Without separation, these compounds were converted into dichloranhydrides of the corresponding pyrimidyl-4-amidophosphoric acids of their hydrochlorides by the action of anhydrous formic acid.

It is well known [1] that trichlorophosphazosulfaniles, trichlorophosphazocarbacyls, and monomeric trichlorophosphazoaryls, by the action of aqueous formic or acetic acid, form dichloranhydrides of the corresponding amidophosphoric acids. During the reaction between anhydrous formic acid and the 2-trichlorophosphazopyrimidines, products of the interaction of heterocyclic amines (2-aminopyrimidines) with phosphorus pentachloride, high yields of highly pure dichloranhydrides of pyrimidil-2-amidophosphoric acid [2] are formed. Certain dichloranhydrides of pyrimidyl-4-amidophosphoric acids have been obtained in a similar manner [3].

In this work it was shown that the formation of dichloranhydrides of pyrimidyl-4-amidophosphoric acids by the interaction between the corresponding 4-trichlorophosphazopyrimidines and anhydrous formic acid is a general method. In addition to anhydrous formic acid it is possible to use anhydrous acetic acid for this purpose. 4-Trichlorophosphazopyrimidines of compound II or hydrochlorides of compound IIa formed from 4-aminopyrimidines and $PCl_5$ in boiling benzene are treated without separation with anhydrous formic acid and the dichloranhydrides of the corresponding pyrimidyl-4-amidophosphoric acids (III) or their hydrochlorides



By the interaction between phosphorus oxychloride and the 4-aminopyrimidines or the corresponding hydrochlorides the acid chlorides were also obtained.

Compound III hydrolyzes in the presence of air and on boiling in water it is converted into the original amines or their hydrochlorides. The compounds IIIa obtained from the lower bases of compound I is rapidly hydrolyzed by water with the formation of compound III, and those formed from the higher bases of compound I dissolve in water with a strong acid reaction. All dichloranhydrides of compound IIIa are hydrolyzed to the original amines on heating in water.

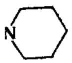
## EXPERIMENTAL

**General method for obtaining the dichloranhydrides of pyrimidyl 4-aminophosphoric acids.** A suspension of 0.02 mole of the corresponding 4-aminopyrimidine and 0.02 mole of $PCl_5$ in 60 ml of benzene were boiled in a stream of nitrogen with mixing until evolution of hydrogen chloride ceased. The resultant solution* of 4-trichlorophosphazopyrimidine or the suspension of the hydrochloride was cooled, and at 15–20° C a solution of 0.02 mole anhydrous formic acid in 10 ml ether was added. After addition of the acid, the reaction mixture was stirred for a further 2 hr at 20° C and left overnight. The precipitate of compound III or IIIa was removed by filtration. The mother liquor was evaporated

---

*The solution was purified with activated carbon whenever necessary.

## Dichloranhydrides of Pyrimidyl-4-Amidophosphoric Acids*

| R′ | R″ | R‴ | pKa[2*] of the original amide | Solvent; temperature, °C; time of the reaction, hr | Melting point, °C (solvent for crystallization) | Empirical formula | Cl, % |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  |  | found | calculated |  |
| Cl | H | Cl | <3 | Benzene; 80; 2.5<br>$POCl_3$; 105; 6 | 146—149 (Benzene) | $C_4H_2Cl_4N_3OP$ | 50.44 | 50.47 | 96.2<br>88 |
| $OCH_3$ | H | Cl | <3 | Benzene; 80; 2 | 145—147[3*] (Ether) | $C_5H_5Cl_3N_3O_2P$ | 38.67 | 38.48 | 95.5 |
| $OCH_3$ | H | $OCH_3$ | 3.22 | Benzene; 80; 2 | 151—152[3*] (Ether) | $C_6H_8Cl_2N_3O_3P$ | 25.21 | 26.07 | 92.4 |
| $CH_3$ | H | $OCH_3$ | 4.42 | Benzene; 80; 1.5 | 176—177 (170)[4*] (Ether) | $C_6H_8Cl_2N_3O_2P$ | 27.75 | 27.70 | 77.2 |
| H | Br | H | 3.15 | Benzene; 80; 3 | 172—174 (Precipitation with ether from acetone) | $C_4H_3BrCl_2N_3OP$ | 24.73 | 24.38 | 96 |
| $CH_3$ | Br | H | 4.08 | Benzene; 80; 3 | 180—183 (172)[4*] (Benzene) | $C_5H_5BrCl_2N_3OP$ | 23.14 | 23.26 | 92 |
| H | Br | $CH_3$ | 3.64 | Benzene; 80; 2.5 | 170—171.5 (Ether) | $C_5H_5BrCl_2N_3OP$ | 23.35 | 23.26 | 88.5 |
| Cl | H | H | <3 | Benzene; 80; 2 | 147—150[3*] | $C_4H_3Cl_3N_3OP \cdot HCl$ | 50.13 | 50.60 | 82.5 |
| $CH_3$ | H | $CH_3$ | 6.4 | Chlorobenzene; 90; 2 | 164[3*] | $C_6H_8Cl_2N_3OP \cdot HCl$ | 38.41 | 38.46 | 91 |
| $CH_3$ | H | H | 5.89 | Chlorobenzene; 130; 1 | 164—166[3*] (150)[4*] | $C_5H_6Cl_2N_3OP \cdot HCl$ | 39.68 | 40.53 | 89.2 |
| H | H | $CH_3$ | 5.5 | Benzene; 80; 2<br>$POCl_3$; 105; 5.5 | 185—186<br>149—151 | $C_5H_6Cl_2N_3OP \cdot HCl$<br>$C_5H_6Cl_2N_3OP$ | 40.42<br>31.39 | 40.53<br>31.38 | 95.4<br>85 |
| H | H |  | 5.85 | Benzene; 80; 1.5<br>$POCl_3$; 105; 2.5 | 162—163 (150)[4*]<br>176—177 (175)[4*] | $C_9H_{13}Cl_2N_4OP \cdot HCl$<br>$C_9H_{13}Cl_2N_4OP$ | 31.93<br>23.74 | 32.08<br>24.03 | 78.4<br>90.2 |

---

*Compounds readily soluble in chloroform less readily soluble in ether and benzene.

[2*] The determination was made by I. V. Persianova.

[3*] Disociation temperature.

[4*] Temperature at which the capillary was introduced into the apparatus.

and an additional quantity of the corresponding compound III was obtained. The precipitate of compound IIIa was washed with acetone and ether.

**Dichloranhydride of 2-chloropyrimidyl-4-amidophosphoric acid.** A suspension of 0.015 mole of 4-amino-2-chloropyrimidine and 0.015 mole of $PCl_5$ in 80 ml of benzene was boiled for 2 hr in a current of nitrogen, and then the reaction mass was cooled, shaken with carbon, filtered, and subsequently treated as indicated above.

**Dichloranhydride of 2, 6-dichloropyrimidyl-4-amidophosphoric acid.** A suspension of 2 g (0.0127 mole) of 4-amino-2, 6-dichloropyrimidine in 12 ml (0.132 mole) of phosphorus oxychloride was boiled for 6 hr, and then excess of phosphorus oxychloride was distilled off under vacuum, the residue was washed with petroleum ether, and 3.09 g (88%) of the dichloranhydride was obtained identical to the corresponding derivative of compound III.

**Dichloranhydride of 6-methylpyrimidyl-4-amidophosphoric acid.** A suspension of 2 g (0.01375 mole) of the hydrochloride of 4-amino-6-methylpyrimidine in 30 ml (0.329 mole) of phosphorus oxychloride was boiled for 5.5 hr, and then the reaction mixture was cooled, the precipitate was removed by filtration, washed with ether, iced water, acetone and ether, and dried in a vacuum dessicator over phosphorus pentoxide. Yield, 85%.

The dichloranhydride of 6-piperidinopyrimidyl-4-aminophosphoric acid was obtained in an analogous manner.

## REFERENCES

1. G. I. Derkach, I. N. Zhmurova, A. V. Kirsanov, V. I. Shevchenko, and A. S. Shtepanek, Phosphazocompounds [in Russian], Naukova dumka, Kiev, 1965.
2. A. A. Kropacheva and N. V. Sazonov, KhGS [Chemistry of Heterocyclic Compounds], 433, 1965.
3. N. V. Sazonov and A. A. Kropacheva, KhGS [Chemistry of Heterocyclic Compounds], 1, 377, 1967.

19 February 1968

Ordzhonikidze All-Union Scientific-Research Institute of
Pharmaceutical Chemistry, Moscow