SYNTHESIS OF AMIDE DERIVATIVES OF PHENOPHOSPHAZINOIC AND THIOPHENOPHOSPHAZINOIC ACIDS

I. V. Cheplanova and D. Kh. Yarmukhametova

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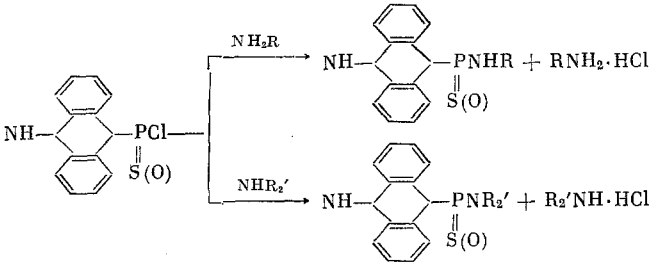
Studies in the domain of the organophosphorus derivatives of phenothiazine [1] and phenoxazine [2], and the detection of anthelmintic properties for a number of these derivatives, led us to synthesize and study the chemical and biological properties of some phenophosphazine derivatives. Besides this, in a British patent [3] it was indicated that various phenophosphazinoic chlorothionates are intermediate products in the synthesis of anthelmintic compounds.

We reacted the acid chlorides of the thiophenophosphazinoic and phenophosphazinoic acids with various amines as described in [4]. The reaction goes under mild conditions in satisfactory yields, forming crystalline compounds that are either white or slightly yellow (in the case of the thio compounds), and are insoluble in water, difficultly soluble in most organic solvents, and soluble in hot ethanol



The starting acid chlorides of the phenophosphazinoic and thiophenophosphazinoic acids were obtained as described in [4], while phenophosphazine was obtained as described in [5].

The obtained compounds are nontoxic toward warm-blooded animals (the LD_{50} is greater than 1000 mg/kg). The anthelmintic activity of the compounds is being studied.

TABLE 1 R=NH— 

Formula	Mp, °C	Found, %		Calculated, %		Yield, %
		P	N	P	N	
RP (S)N $(C_2H_5)_2$	184—18	10,40	9,28	10,20	9,30	40,0
RP (S)NHC$_3$H$_7$	238—23	10,49	10,0	10,70	9,70	60,0
RP (S)NHC$_3$H$_5$	251—25	10,82	9,94	10,83	9,78	50,0
RP (S)NHCH$_2$CH$_2$OH	185—18	10,73	10,0	10,68	9,94	40,0
RP (S)NHC$_6$H$_5$	238—240	9,72	8,86	9,62	8,69	40,0
RP (O)N $(C_2H_5)_2$	244—24	10,69	9,72	10,80	9,78	57,0
RP (O)NHC$_3$H$_7$	254—25	11,63	10,27	11,40	10,28	51,5
RP (O)NHC$_4$H$_9$	238—23	10,60	9,78	10,8	9,87	50,0
RP (O)NHC$_3$H$_5$	254—25	11,65	10,45	11,50	10,36	51,0
RP (O)NHCH$_2$CH$_2$OH	232—23	11,50	10,23	11,31	10,20	52,0
RP (O)NHC$_6$H$_5$	241—24	9,72	9,03	10,1	9,14	54,0

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EXPERIMENTAL

Propylamide of Thiophenophosphazinoic Acid. In a three-necked flask, fitted with a stirrer and a reflux condenser, was placed 10 ml of propylamine, and 1.3 g of thiophenophosphazinoyl chloride was added in drops. The mixture was stirred at room temperature for 1 h and at amine reflux for 1 h in order to complete the reaction. Then to the stirred mixture, with cooling, was added a small amount of chilled water. The water-insoluble precipitate was filtered, washed with water, and dried. The weight of crude product was 1.3 g (90%). After recrystallization from ethanol we obtained 0.8 g (60%) of crystalline substance with mp 238-239°.

The reactions of the acid chlorides with diethylamine, allylamine and monoethanolamine were run in a similar manner.

Anilide of Phenophosphazinoic Acid. In a three-necked flask, fitted with a stirrer and a reflux condenser, was placed 10 ml of aniline, and 1.5 g of phenophosphazinoyl chloride was added in drops. Noticeable warming up was observed. The mixture was stirred at room temperature for 15 min and then heated (bath temperature 80-85°) for 4 h. The precipitate was filtered, washed several times with ether and then with small portions of chilled water. The weight of the precipitate was 1.85 g (100%). Recrystallization from ethanol gave 1 g (54%) of crystalline substance with mp 241-242°.

The reaction of thiophenophosphazinoyl chloride with aniline was run in a similar manner.

The constants and analyses of the obtained compounds are given in Table 1.

CONCLUSIONS

Ten new amides of the phenophosphazinoic and thiophenophosphazinoic acids were synthesized.

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