ORGANOPHOSPHORUS DERIVATIVES OF PENTACHLOROPHENOL

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D. Kh. Yarmukhametova and I. V. Cheplanova

A. E. Arbuzov Chemical Institute, Academy of Sciences of the USSR

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Among the numerous compounds with biological activity, and fungicidal activity in particular, pentachlorophenol and its various derivatives are beginning to become important. For example, mixed carbonic esters containing pentachlorophenyl groups have been proposed for use as fungicides [1]. A number of pentachlorophenyl esters of fatty acids have been shown to have fungistatic activity [2].

Chloroacetic esters containing a pentachlorophenyl group act as a contact poison for "resistant" flies [5]. A 2% emulsion of pentachlorophenyl vinyl ether destroys the eggs of the mites which infest apple trees and poplars [4]. Aryl benzenesulfonates, in which aryl = tri-, tetra-, or pentachlorophenyl, have acaricidal and ovicidal properties against the red citrus mite and other insects [5]. A good fungicide is methylmercury pentachlorophenoxide, which is used for the destruction of spores of fungi producing rot in wheat [6].

In the patent literature there are some references to the preparation of some organophosphorus derivatives of pentachlorophenol and their fungicidal and insecticidal properties [7-9]. It is stated in the literature [10] that some pentachlorophenol derivatives have phytotoxic as well as fungicidal and insecticidal properties.

We have synthesized some phosphoric, phosphorous, and phosphorothioic esters containing pentachlorophenyl groups for the purpose of studying their fungicidal and insecticidal properties. We prepared phosphoric and phosphorothioic esters containing one and two pentachlorophenyl groups. Dialkyl pentachlorophenyl phosphates were synthesized by the reaction of pentachlorophenol with dialkyl phosphorochloridates in presence of triethylamine:

$$\begin{gathered} C_6Cl_5OH + ClP(O)(OR)_2 + Et_3N \rightarrow \\ \rightarrow C_6Cl_5OP(O)(OR)_2 + Et_3N\cdot HCl, \\ \text{where } R = CH_3;\ C_2H_5;\ i\text{-}C_3H_7;\ C_4H_9 \end{gathered}$$

The constants and yields of the products are listed in the table [(I)-(IV)]. By the reaction of pentachlorophenol with ethyl and butyl phosphorodichloridates we obtained ethyl and butyl bispentachlorophenyl phosphates (V) and (VI). Apart from the phosphoric esters we synthesized phosphoramidic esters containing pentachlorophenyl groups by the reaction of pentachlorophenol with phosphoramidochloridates [(VII)-(IX)]. We prepared also tervalent phosphorus esters by the reaction of pentachlorophenol with the corresponding acid chlorides [(X) and (XI)]. The addition of sulfur to diethyl pentachlorophenyl phosphite occurred readily with formation of diethyl pentachlorophenyl phosphorothioate.

The physical constants of the latter agreed closely with those of the product that we obtained in the reaction of pentachlorophenol with O,O-diethylphosphorochloridothioate [see (XII) in table]. Attempts to bring about the addition of sulfur to ethyl bispentachlorophenyl phosphite were unsuccessful. Sulfur could not be caused to add to this phosphite either in solvents (benzene, xylene) at the boil or by direct interaction in the melt.

Attempts were made to bring about the Arbuzov rearrangement of diethyl pentachlorophenyl phosphite under the action of alkyl halides. The reaction of diethyl pentachlorophenyl phosphite with ethyl bromide in sealed tubes at 135-140° for 5 h did not go. The starting substances were recovered. In the reaction of diethyl pentachlorophenyl phosphite with benzyl chloride the situation was similar. When the reaction was carried out under more severe conditions (heating at 170° for 6 h), the product decomposed.

No.	Formula	M.p., °C	Found, %		Calc., %		Yield, % of	
			P	Cl	P	Cl	crude product	recryst. product
I	$C_6Cl_5OP(O)(OCH_3)_2$	137— 139	8,23 8,31	47,38 47,60	8,23	47,4	≈100	70
II	$C_6Cl_5OP(O)(OC_2H_5)_2$	115— 116	8,05 7,94	44,05 44,24	7,7	44,1	99,0	73,7
III	$C_6Cl_5OP(O)(OC_3H_7\text{-}i)_2$	81	7,4 7,5	41,94 41,82	7,21	41,23	99,8	62,8
IV	$C_6Cl_5OP(O)(OC_4H_9)_2$	50— 52	6,76 6,75	38,47	6,76	38,71	99	39,2
V	$(C_6Cl_5O)_2P(O)OC_2H_5$	158— 159	5,18 5,18	56,80 57,0	4,97	56,98	98,9	60,0
VI	$(C_6Cl_5O)_2P(O)OC_4H_9$	143	4,96 4,89	54,25 54,30	4,76	54,53	84,6	47
VII	$C_6Cl_5OP(O)[N(CH_3)_2]_2$	143— 144	7,93 7,78	44,40	7,74	44,3	99,2	64,3
VIII	$(C_6Cl_5O)_2P(S)N(CH_3)_2$	216— 217	5,02 5,03	55,55 55,23	4,86	55,64	40	21
IX	$(C_6Cl_5O)_2P(O)N(CH_3)_2$	180— 182	5,13 5,21	56,52 56,77	4,98	57,1	84,4	52,3
X	$C_6Cl_5OP(OC_2H_5)_2$	37	8,05 8,03	45,50 45,50	8,0	45,9	93,3	59,5
XI	$(C_6Cl_5O)_2POC_2H_5$	135— 137	5,17 5,19	58,60 58,80	5,1	58,5	≈100	70
XII	$C_6Cl_5OP(S)(OC_2H_5)_2$	96— 97 97— 98	7,27 7,40 7,68 7,55	42,47 42,23 42,70	7,4 7,4	42,4 42,4	98,3 ≈100	58,4* 41,0**

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* By the addition of sulfur.

* * By reaction of pentachlorophenol with the acid chloride.

In an attempt to carry out the Arbuzov rearrangement of diethyl pentachlorophenyl phosphite with acetyl bromide, somewhat unexpected results were obtained. We isolated ethyl bromide in 50% yield and a pure substance, which melted sharply at 149-150° and did not contain phosphorus, in 23% yield; according to analysis and the melting point, this was pentachlorophenyl acetate [11]. The residue was a resinous mass containing phosphorus. In the course of this work we developed a method for the preparation of pentachlorophenol under laboratory conditions.

Preliminary tests on one of the esters obtained, namely diethyl pentachlorophenyl phosphate, showed that it is of low toxicity to warm-blooded animals and has only slight insecticidal activity toward the corn weevil. We are at present carrying out more detailed tests for biological activity on the preparations obtained.

EXPERIMENTAL

Preparation of Pentachlorophenol. There are references in the patent literature to the preparation of pentachlorophenol by the chlorination of phenol in presence of catalysts [12]. We carried out the chlorination as follows. Weighed amounts of phenol (46.5 and 44.8 g) were introduced into two elongated flasks fitted with a bubbler for chlorine and a thermometer. Chlorine was passed through the first flask at 40-50°, when the phenol was chlorinated to trichlorophenol. When this process was complete (checked by the increase in weight), 1.5 g of $AlCl_3$ catalyst was added (about 3% on the phenol). Chlorination was continued in the first flask containing the catalyst, and the temperature was raised gradually to 90° and finally to 135-140°. Excess chlorine from the first flask was passed into the second flask, in which the chlorination of phenol to trichlorophenol was carried out at 50°. At the end of the chlorination (checked by the increase in weight), the reaction mixture from the first flask was treated with 5% sodium hydroxide solution, and the aqueous solution of sodium pentachlorophenoxide was acidified with hydrochloric acid, which resulted in the formation of a precipitate of pentachlorophenol. We obtained 105 g (80%) of this precipitate, m.p. 178°. Crystallization from benzene gave 52 g of pentachlorophenol, m.p. 186°. Found: C 26.7, 26.8; H 0.7, 0.8; Cl 66.2, 66.1%. C_6HOCl_5. Calculated: C 26.01; H 0.4; Cl 66.6. From the mother liquor, after steam distillation, we obtained a further 25 g of the substance. Total yield 74%.

Synthesis of Dimethyl Pentachlorophenyl Phosphate. A mixture of 8 g of pentachlorophenol, 3.5 g of triethylamine, and 60 ml of benzene was prepared in a three-necked flask fitted with stirrer, dropping funnel, and reflux condenser. 4.34 g of dimethyl phosphorochloridate was then added gradually at room temperature. Triethylamine hydrochloride was filtered off and solvent was driven off, and we then obtained 11 g of crystals. Crystallization from gasoline (70-100°) gave 7.7 g (70%) of dimethyl pentachlorophenyl phosphate, m.p. 137-139°, in the form of white crystals, insoluble in water, but soluble in ether, benzene, chloroform, and carbon tetrachloride.

Synthesis of Diethyl Pentachlorophenyl Phosphate. The procedure was similar to that described above. We took 1.3 g of pentachlorophenol, 0.5 g of triethylamine, 0.84 g of diethyl phosphorochloridate, and 30 ml of dry ether. We obtained 1.9 g (99%) of yellow crystals, m.p. 113-115°. By the crystallization of the latter from a 1:1 mixture of alcohol and water we obtained 1.4 g (73.7%) of diethyl pentachlorophenyl phosphate, m.p. 115-116°, in the form of white crystals, insoluble in water, but soluble in ether, benzene, and other organic solvents.

Preparation of Diisopropyl Pentachlorophenyl Phosphate. The procedure was similar to that described above. We took 5.3 g of pentachlorophenol, 2.1 g of triethylamine, and 4 g of diisopropyl phosphorochloridate. We separated 2.7 g (98.2%) of triethylamine hydrochloride. The crude product isolated amounted to 8.6 g (99.5%). We were unable to purify it by recrystallization. 7 g of the substance was shaken with 27 g of alumina in petroleum ether. We obtained 4.4 g (63%) of hexagonal prisms, m.p. 81°, soluble in ether, benzene, and many other organic solvents.

Preparation of Dibutyl Pentachlorophenyl Phosphate. The procedure was similar to that described above. We took 5.3 g of pentachlorophenol, 2.1 g of triethylamine, and 4.6 g of dibutyl phosphorochloridate. Triethylamine hydrochloride was separated (quantitative yield). Solvent was removed, and we obtained 9.1 g (99.2%) of product. Its purification was effected as in the preceding experiment. From 6.9 g of crude product (shaken with 33 g of alumina) we obtained 2.7 g (39.3%) of colorless crystals, m.p. 50-52°, insoluble in water, but soluble in ether, benzene, and other organic solvents.

Synthesis of Ethyl Bispentachlorophenyl Phosphate. For reaction we took 5.33 g of pentachlorophenol, 2.2 g of triethylamine, and 1.63 g of ethyl phosphorodichloridate. The procedure was analogous to that described above. Benzene was used as solvent. Triethylamine hydrochloride was isolated quantitatively. The product was recrystallized from ethyl acetate. We obtained 3.7 g (60%) of a substance of m.p. 158-159°.

Synthesis of Butyl Bispentachlorophenyl Phosphate. The procedure was similar to that described above. For reaction we took 10.66 g of pentachlorophenol, 4.4 g of triethylamine, and 3.8 g of butyl phosphorodichloridate. 11 g (84.6%) of triethylamine hydrochloride was isolated. After recrystallization from ethyl acetate we obtained 6.1 g (47%) of product, m.p. 143°.

Synthesis of Pentachlorophenyl N,N,N',N'-Tetramethylphosphorodiamidate. For reaction we took 5.33 g of pentachlorophenol, 2.2 g of triethylamine, and 3.4 g of N,N,N',N'-tetramethylphosphorodiamidic chloride. The reaction was carried out in benzene. 2.35 g (85.5%) of triethylamine hydrochloride was separated. The product formed yellow crystals which, after being washed with ether, amounted to 5.2 g (64.4%); m.p. 143-144°.

Synthesis of Bispentachlorophenyl N,N-Dimethylphosphoramidate. For reaction we took 10.66 g of pentachlorophenol, 4.4 g of triethylamine, and 3.24 g of N,N-dimethylphosphoramidic dichloride. Triethylamine hydrochloride was isolated quantitatively. After the removal of solvent we isolated 14 g of yellow crystals, which were washed with dry ether. Crystallization of the resulting crystals (10.5 g) from ethyl acetate gave 6.5 g (52.3%) of crystals of m.p. 180-183°, insoluble in water, acetone, and ether, but soluble in benzene.

Synthesis of O,O-Bispentachlorophenyl N,N-Dimethylphosphoramidothioate. For reaction we took 10.66 g of pentachlorophenol, 4.4 g of triethylamine, and 3.56 g of N,N-dimethylphosphoramidothioic dichloride. The reaction was carried out in toluene, and the procedure was similar to that described above. Heating was for 6 h. 4.1 g (74.5%) of triethylamine hydrochloride was isolated. The removal of toluene left 14.8 g of residue, which crystallized out after 3 weeks. The resinous crystals were washed with ether, and we isolated 5 g of product, which was recrystallized from ethyl acetate. 2.6 g (21%) of pure O,O-bispentachlorophenyl N,N-dimethylphosphoramidothioate was isolated. It was insoluble in water, but soluble in benzene; m.p. 216-217°.

Preparation of Diethyl Pentachlorophenyl Phosphite. For reaction we took 13.3 g of pentachlorophenol, 5.2 g of triethylamine, and 7.8 g of diethyl phosphorochloridate. The reaction was carried out in ether at room temperature by a procedure analogous to that described above. 6.5 g (94.2%) of triethylamine hydrochloride was isolated. The crude product amounted to 18 g (93.3%) and it was purified by distillation from an Arbuzov flask. We obtained 11.8 g (59.5%); b.p. 150-152° (0.5 mm); m.p. 37°; insoluble in water; readily soluble in ether and benzene.

Preparation of Ethyl Bispentachlorophenyl Phosphite. For reaction we took 10.6 g of pentachlorophenol, 4.3 g of triethylamine, and 3 g of ethyl phosphorodichloridate. The reaction was carried out in benzene by a procedure analogous to that described above. Triethylamine hydrochloride was isolated quantitatively. The weight of product after the removal of solvent was 12 g (98.8%). This was washed with cold absolute methanol to remove resin, which left 7 g (58%). Recrystallization from gasoline gave a product of m.p. 134-135°.

Synthesis of O, O-Diethyl O-Pentachlorophenyl Phosphorothioate. 0.5 g of sulfur was added in small portions to a melt of 3.85 g of diethyl pentachlorophenyl phosphite at 40° in a round-bottomed flask provided with a thermometer. The contents of the flask were heated at 120° for 4 h. When cooled, the whole mass solidified. The product was crystallized from ethanol, and we obtained 2.5 g (61%) of a substance of m.p. 96-97°. The product was insoluble in water, but soluble in ether, benzene, and other organic solvents.

From 3.1 g of pentachlorophenol, 1.5 g of triethylamine, and 2.3 g of O, O-diethylphosphorochloridothioate in benzene by reaction under the conditions described above, we obtained, after the removal of solvent, 5 g of crystalline product. Recrystallization from alcohol gave 2 g (41%) of crystals of m.p. 97-98°; a mixture of this product with the product obtained directly by the addition of sulfur to the phosphite had m.p. 97-98°.

Reaction of Diethyl Pentachlorophenyl Phosphite with Acetyl Bromide. The reaction was carried out in a three-necked flask fitted with condenser set for distillation, stirrer, dropping funnel, and thermometer. For reaction we took 7.3 g of diethyl pentachlorophenyl phosphite, and to this in the molten condition 2.3 g of acetyl bromide was added dropwise. The contents of the flask were then heated at 110-130° for 4 h. Ethyl bromide (0.7 ml) was then driven off. When cool, the contents of the flask solidified. By recrystallization from methanol we obtained 1.4 g of crystals of m.p. 149-150°. The residue was a viscous resinous mass. Analysis showed the absence of phosphorus. The results of analysis and the melting point* indicate that the product was pentachlorophenyl acetate. Found: C 31.23; 31.26; H 1.19, 1.17; Cl 58.2%. $C_8H_3O_2Cl_5$. Calculated: C 31.1; H 0.97; Cl 57.5.

SUMMARY

Twelve phosphorus esters containing one or two pentachlorophenyl groups were prepared for the purpose of studying their insecticidal and fungicidal activity.

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*The literature gives m.p. 149.5-150.5°.