PREPARATION AND ISOMERIZATION OF DIALKYL, DIARYL, AND ALKYLENE 2-(2-CHLOROETHOXY)-1-(CHLOROMETHYL)ETHYL PHOSPHITES

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Chlorine-substituted mixed phosphorous esters having an open chain tend to undergo redistribution of the phosphorus-attached alkoxyls. In the fractionation of the product of the reaction of 2-chloroethyl phosphorodichloridite with ethanol Kabachnik and Rossiiskaya [1] isolated triethyl phosphite, 2-chloroethyl diethyl phosphite, bis-2-chloroethyl ethyl phosphite, and tris-2-chloroethyl phosphite. The redistribution of the alkoxyls at a phosphorus atom was observed also by Pudovik and Ivanov [2] in the fractionation of products of the reaction of diethyl phosphorochloridite with ethylene oxide and with 2,3-epoxybutane. When distilled, dialkyl 2-chloro-1-(chloromethyl)ethyl phosphites also undergo redistribution of alkoxyls [3]. An exception is formed by chlorine-substituted t-alkyl mixed phosphorous esters [4], which show no tendency to undergo redistibution of groups.

We carried out the reaction of phosphorus trichloride with 1-chloro-3-(2-chloroethoxy)-2-propanol, prepared by the method of Fourneau and Ribas [5]. In the reaction between equimolecular proportions of the reactants we isolated 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphorodichloridite and bis[2-(2-chloroethoxy)-1-(chloromethyl)-ethyl] phosphorochloridite. We studied the reaction of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphorodichloridite with aliphatic alcohols, with phenol, and with diols. The reactions were carried out in presence of triethylamine in an anhydrous ether medium. We then obtained mixed phosphorous esters, whose constants are listed in Table 1.

The relatively low yields of the mixed phosphorous esters are to be explained by the redistribution of phosphorus-attached alkoxyls. On fractionation of the crude reaction products we isolated low-boiling fractions, partly in a trap cooled with liquid nitrogen and partly as the head fraction. In most cases we were unable to isolate pure products boiling over narrow temperature ranges by the redistillation of these fractions. Only in the fractionation of the low-boiling fraction obtained in the distillation of crude 2-(2-chloroethoxy)-1-(chloromethyl)ethyl diisopropyl phosphite were we able to isolate triisopropyl phosphite. After mixed phosphorous esters had been distilled off, in all cases there remained considerable amounts of sirupy substances in the distilling flask, and we were unable to establish the compositions of these. In the case of the distillation of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dipentyl and diisopentyl phosphites, their isomerization products were isolated (Table 2, No. 7 and 8). When distilled, 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dihexyl phosphite was isomerized to a considerable extent. Thus, in the distillation of the crude product we isolated only 16% of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dihexyl phosphite and 36% of its isomerization product. 2-(2-Chloroethoxy)-1-(chloromethyl)ethyl diphenyl phosphite is isomerized to a less extent when distilled.

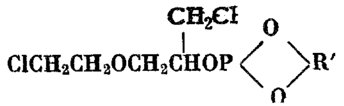
It should be noted that the mixed esters that we obtained largely underwent redistribution of alkoxyls when distilled. Thus, in the fractional distillation of 40 g of crude 2-(2-chloroethoxy)-1-(chloromethyl)ethyl diethyl phosphite (at 13 mm with a bath temperature of 190°) we isolated triethyl phosphite (7 g), and the yield of mixed phosphorous ester was only 4.5 g. All the mixed phosphorous esters obtained were colorless viscous liquids, soluble in organic solvents, but sparingly soluble in water. The phosphite odor weakened with rise in molecular weight.

Cyclic mixed phosphorous esters (see Table 1, No. 9, 10, 11, and 12) were prepared by the reaction of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphorodichloridite with diols in presence of triethylamine. The yields of esters were low. In all cases very thick colorless substances remained in the distilling flask: these were probably polymerization products. All the mixed phosphorous esters that we obtained reacted exothermically with cuprous chloride [6] and gave noncrystallizing resinous complex compounds.

TABLE 1. Dialkyl, Diaryl, and Cyclic Alkylene 2-(2-Chloroethyl)-1-(chloromethyl)ethyl Phosphites

$ClCH_2CH_2OCH_2\overset{\displaystyle CH_2Cl}{\overset{|}{C}}HOP(OR)_2$

and



No.	R, R′	B.p., °C (p, mm)	d_4^{20}	n_D^{20}	*MR*		Cl, %		P*, %		Yield, %
					found	calc.	found	calc.	found	calc.	
1	R = CH_3	90—92 (0,5)	1,2550	1,4688	58,80	59,02	26,60	26,75	11,35	11,69	62,5
2	C_2H_5	96—98 (0,15)	1,1830	1,4622	68,15	68,26	24,21	24,20	10,47	10,57	62,5
3	C_3H_7	119—120 (0,18)	1,1380	1,4614	77,65	77,49	22,30	22,09	9,86	9,65	76,3
4	*i*-C_3H_7	111—112 (0,18)	1,1270	1,4558	77,44	77,49	22,00	22,09	9,80	9,65	53,0
5	C_4H_9	139—140 (0,18)	1,1090	1,4612	86,48	86,73	20,32	20,30	8,70	8,88	67,5
6	*i*-C_4H_9	134—135 (0,19)	1,0980	1,4580	86,75	86,73	20,17	20,30	8,64	8,88	49,0
7	C_6H_{13}	163—165 (0,012)	1,0450	1,4583	105,90	105,20	—	—	7,43	7,66	16,0
8	C_6H_5	173—174 (0,013)	1,2590	1,5485	98,22	98,02	18,53	18,23	17,62	17,96	49,5
9	R′ = $-CH_2-CH_2-$	110—112 (0,22)	1,3420	1,4893	55,62	56,82	26,46	26,95	1,33	1,77	55,0
10	$-\overset{\displaystyle CH_3}{\overset{|}{C}}H-CH_2-$	107—108 (0,075)	1,2890	1,4820	61,27	61,44	25,60	25,60	10,82	11,18	71,0
11	$-\overset{\displaystyle CH_2Cl}{\overset{|}{C}}H-CH_2-$	128 (0,11)	1,3900	1,5000	65,93	66,31	33,97	34,12	9,73	9,94	55,5
12	$-C(CH_3)_2-C(CH_3)_2-$	134—183 (0,18)	1,2000	1,4725	74,62	75,29	22,46	22,21	9,86	9,70	34,2

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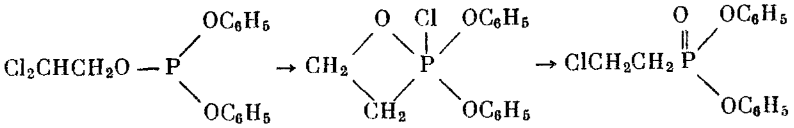
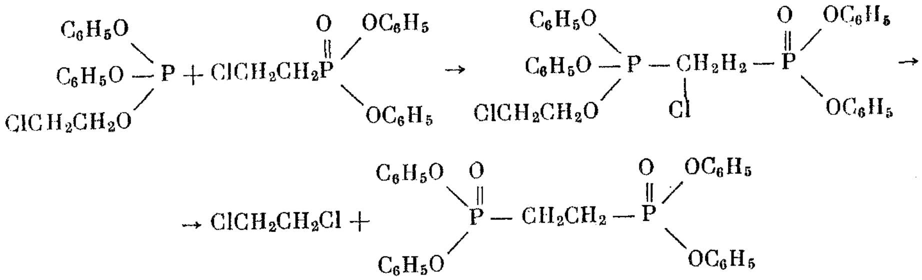
* The chlorine and phosphorus contents are means of two determinations.

The isomerization of mixed phosphorous esters by means of alkyl halide occurs with elimination of the unsubstituted alkyl. Thus, by heating 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dimethyl phosphite with methyl iodide we obtained 2-(2-chloroethoxy)-1-(chloromethyl)ethyl methyl methylphosphonate in 67.5 % yield. The thermal isomerization of the mixed phosphorous esters that we prepared went in a complex manner. Kabachnik [7] showed that in the course of repeated distillation tris-2-chloroethyl phosphite is converted into bis-2-chloroethyl 2-chloroethylphosphonate in accordance with the scheme previously proposed by the author. By heating 2-chloroethyl diphenyl phosphite to 250°, Kabachnik [8] obtained tetraphenyl ethylenediphosphonate. He gives a scheme for the formation of this ester. In the first place:

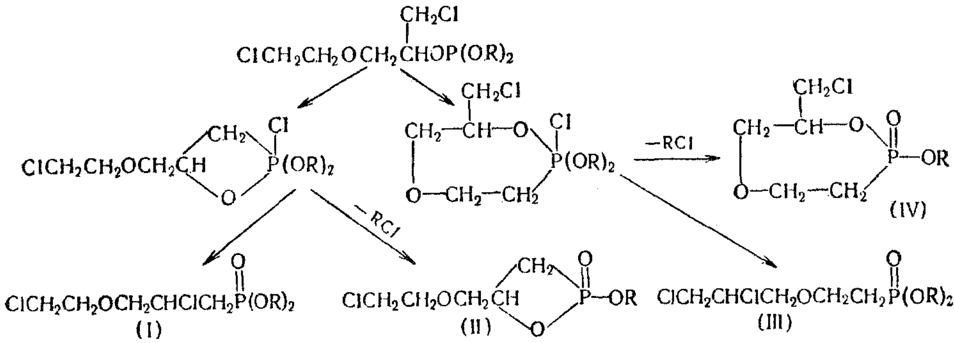


The diphenyl 2-chloroethylphosphonate formed then reacts with a second molecule of the phosphorous ester by the Arbuzov scheme [6]:



The extreme ease with which chlorine-substituted phosphorous esters are isomerized was observed by Rizpolozhenskii and Muslinkin [9] and later by Pudovik and Faizullin [10]. A dialkyl 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphite can, on being heated, theoretically give two intramolecular-isomerization products (I) and (III) together with two other products (II) and (IV), whose composition will differ from that of the original phosphorous ester. Moreover, as a result of the reaction of the products (I), (II), (III), and (IV) with a second phosphorous ester molecule, compounds of higher molecular weight may be formed.

We carried out the isomerization of mixed phosphorous esters by heating them in p-dichlorobenzene or by heating them in sealed tubes in absence of solvent. As a result we obtained various dichloro-substituted phosphonic esters, the constants of which are given in Table 2.



With the object of determining the structure of the chlorine-substituted group of the phosphonic ester (I) or (III), we heated the dipropyl dichloro-substituted phosphonate (Table 2, No. 3) with zinc dust. We recovered the original ester unchanged. This phosphonic ester also remained unchanged when it was heated with silver oxalate. Although the inertness of the dichloro phosphonic ester toward zinc and silver oxalate is an argument in favor of the structure (I), its structure was not proved.

TABLE 2. Phosphonic Esters of Formula $R'\overset{O}{\overset{\|}{P}}(OR)_2$

$R' = ClCH_2CH_2OCH_2CH(Cl)CH_2-$ or $ClCH_2CH(Cl)CH_2OCH_2CH_2-$

No.	R	B. p., °C (p, mm)	d_4^{20}	n_D^{20}	MR		Cl, % *		P, % *		Yield, %
					found	calc.	found	calc.	found	calc.	
1	CH_3	126—128 (0,15)	1,3130	1,4715	56,48	56,77	26,33	26,60	10,70	11,35	35,0
2	C_2H_5	138—139 (0,16)	1,2350	1,4715	66,40	66,01	24,11	24,20	10,07	10,57	53,0
3	C_3H_7	146—147 (0,12)	1,1830	1,4620	74,62	75,18	21,70	22,09	9,53	9,65	56,0
4	i-C_3H_7	123—124 (0,12)	1,1678	1,4576	75,00	75,18	22,30	22,09	9,45	9,65	46,0
5	C_4H_9	168—169 (0,16)	1,1388	1,4616	84,23	84,48	20,17	20,30	8,57	8,88	55,0
6	i-C_4H_9	151—152 (0,16)	1,1320	1,4585	84,26	84,48	20,03	20,30	8,52	8,88	21,6
7	C_5H_{11} **	164 (0,18)	1,1170	1,4602	92,60	92,71	18,90	18,80	8,16	8,31	26,4
8	i-C_5H_{11}**	143—145 (0,012)	1,1090	1,4606	93,50	92,71	18,82	18,80	8,01	8,21	30,8
9	C_6H_{13} **	191—192 (0,012)	1,0840	1,4612	102,70	102,95	17,02	17,54	7,38	7,66	36,0
10	C_6H_5 **	187—194 (0,013)	1,2780	1,5463	96,45	95,77	18,68	18,23	7,72	7,96	15,4
11	$ClCH_2-\underset{\vert}{CH}-$ CH_2-	—	1,4210	1,5100	64,60	64,08	33,83	34,12	9,20	9,94	—

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* The chlorine and phosphorus contents are means of two determinations.

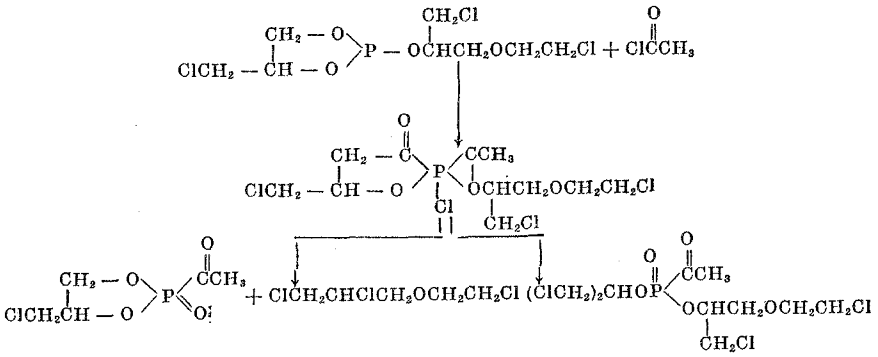
** Obtained in the distillation of the corresponding mixed phosphorous ester.

The low yields of phosphonic esters and the considerable resinous residues left in the distillation of the crude isomerization products do not exclude the possibility of the formation of alkylenediphosphonic esters in accordance with the above-cited scheme of Kabachnik. Also, it is here possible that reaction may proceed with elimination of alkyl halide, which would lead to the formation of the product (II) or (IV).

With the object of ascertaining whether this reaction may occur, we carried out the isomerization of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl diisopropyl and diisobutyl phosphites, which were heated in sealed tubes. When the tube containing the diisopropyl dichloroalkylphosphonate was opened, it was found that the pressure was only slight. In the vacuum fractionation of this product the liquid foamed strongly; readily volatile products were frozen out in the trap cooled with liquid nitrogen, but from these we were unable to isolate any individual products. In the fractionation of the diisobutyl dichloroalkylphosphonate we succeeded in isolating and characterizing isobutyl chloride. Hence, in the cases studied two reactions proceed simultaneously: isomerization, leading to the product (I) or (III), and a reaction proceeding with liberation of alkyl chloride and leading to the product (II) or (IV). We were unable to isolate the product (II) or (IV); it is possible that, on being heated, it suffers a more complex change. The isomerization reaction predominates.

The dipentyl, diisopentyl, dihexyl, and diphenyl dichloroalkylphosphonates (Table 2, No. 7, 8, 9, and 10) were isolated in the distillation of the corresponding crude mixed 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites. An analogous thermoisomerization is observed in the distillation of tris[2-chloro-1-(chloromethyl)ethyl] phosphite [9].

It is known that cyclic phosphorous esters, reacting with carboxylic acid chlorides, may react with or without opening of the ring [11]. On analogy with data in the literature we expected that the reaction of cyclic alkylene 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites with acetyl chloride would go with or without decyclization in accordance with the scheme



From the products of the reaction of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl (chloromethyl)ethylene phosphite with acetyl chloride we isolated (chloromethyl)ethylene phosphorochloridite. This gives us reason to suppose that an exchange reaction occurred. A similar exchange reaction occurs when acetyl chloride acts on antimonous esters [12] and on cyclic arsenious esters [13].

EXPERIMENTAL

Reaction of Phosphorus Trichloride with 1-Chloro-3-(2-chloroethoxy)-2-propanol. A 250 ml flask fitted with thermometer, mechanical stirrer, dropping funnel, and reflux condenser was charged with 80.5 g of phosphorus trichloride and was cooled externally with ice water while 102 g of 1-chloro-3-(2-chloroethoxy)-2-propanol was added dropwise at such a rate that the temperature inside the flask did not exceed 10°. Stirring was then continued at room temperature for one hour. The reaction product was transferred to an Arbuzov flask, and hydrogen chloride was removed in a vacuum. The crude viscous product was distilled in a stream of dry carbon dioxide. We obtained: Fraction I (2.8 g), b.p. up to 235° (8 mm); Fraction II (106.5 g), b.p. 135-136° (8 mm); Fraction III (6.5 g), b.p. up to 178° (0.08 mm); Fraction IV (25.1 g), b.p. 178-179° (0.08 mm); residue (17.2 g).

The fraction of b.p. 135-136° (8 mm) had the constants: d_4^{20} 1.4360; n_D^{20} 1.5108. Found: Cl 51.56; 51.59; P 10.81; 10.66%; MR 57.10. $C_5H_9O_2Cl_4P$. Calculated: Cl 51.76; P 11.33%; MR 56.97. The substance of b.p. 135-136° (8 mm) was therefore 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphorodichloridite, a thick liquid which fumed in air. On hydrolysis with an equivalent amount of water it was converted quantitatively into the corresponding acid ester; d_4^{20} 1.4164; n_D^{20} 1.4800. Found: Cl 29.71; P 12.70%; MR 47.57. $C_5H_{11}O_4Cl_2P$. Calculated: Cl 29.92; P 13.01%; MR 47.42. It was a sirupy odorless liquid.

The product of b.p. 178-179° (0.08 mm) was bis[2-(2-chloroethoxy)-1-(chloromethyl)ethyl] phosphorochloridite; d_4^{20} 1.3900; n_D^{20} 1.5048. Found: Cl 42.73; P 7.97%; MR 87.54. $C_{10}H_{18}O_3Cl_5P$. Calculated: Cl 43.19; P 7.55%; MR 87.85. The total yield of acid chlorides was 86%.

Preparation of Dialkyl, Diaryl, and Alkylene 2-(2-Chloroethoxy)-1-(chloromethyl)ethyl Phosphites. A 500 ml four-necked flask fitted out as described above was charged with 0.4 mole of the appropriate absolute alcohol or phenol, or with 0.2 mole of the diol, and with 0.4 mole of triethylamine and 350 ml of anhydrous ether. The flask was cooled externally with a mixture of snow and salt, and 0.2 mole of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphorodichloridite was added dropwise at such a rate that the temperature inside the flask did not rise above − 3°. Stirring was then continued at room temperature (4-6 hours). Triethylamine hydrochloride was filtered off, and ether was vacuum-distilled off. Distillation of the crude residue from an Arbuzov flask gave mixed 2-(2-chloroethoxy)-1-chloromethyl)ethyl phosphites, the yields and constants of which are listed in Table 1. On distillation of crude 2-(2-chloroethoxy)-1-(chloromethyl)ethyl diisopropyl phosphite we isolated 3.4 g (12%) of triisopropyl phosphite; b.p. 65-67° (12 mm); d_4^{20} 0.9376; n_D^{20} 1.4145. Its complex compound with cuprous chloride, after recrystallization from a 1 : 1 mixture of chloroform and alcohol, melted at 112-114°.

Isomerization of Mixed 2-(2-Chloroethoxy)-1-(chloromethyl)ethyl Phosphites. Isomerization reactions were carried out under identical conditions with 30.0 g of dimethyl, 30.1 g of diethyl, 41.0 g of dipropyl, and 40.0 g of dibutyl 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites. The phosphorous ester and an equal weight of p-dichlorobenzene were placed in a three-necked flask having ground glass joints and fitted with stirrer, thermometer, and reflux condenser protected by a calcium chloride tube. The mixture was heated with stirring at 160-170° for eight hours. p-Dichlorobenzene was distilled off from the same flask at 12 mm, and distillation of the residue from an Arbuzov flask gave the isomerization products, the constants and yields of which are listed in Table 2 (No. 1, 2, 3, and 5).

The isomerization of 13 g of diisopropyl and 13 g of diisobutyl 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites was brought about by heating them at 160-170° in sealed tubes for eight hours. When cool, the tubes were opened and the products distilled from an Arbuzov flask. The constants of the final products are given in Table 2 (No. 4, 6).

In the fractionation of 13 g of the crude product of the isomerization of 2-(chloroethoxy)-1-(chloromethyl)-ethyl diisobutyl phosphite we collected 1.4 g of material in a trap cooled with liquid nitrogen, and by distillation of this we isolated 0.7 g (14%) of isobutyl chloride; b.p. 68-69°; n_D^{20} 1.3962; d_4^{20} 0.8820.

Action of Zinc Dust and of Silver Oxalate on 2-(2-Chloroethoxy)-1-(chloromethyl)ethyl Dipropyl Phosphite. A mixture of 19 g of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dipropyl phosphite, 20 ml of absolute ethanol, and 3.9 g of zinc dust was prepared in a 100 ml flask fitted with stirrer, thermometer, and reflux condenser protected by a calcium chloride tube. The mixture was stirred at 78° for eight hours. No signs of reaction were observed. Zinc was removed and ethanol was distilled off; we recovered 16 g of the mixed phosphorous ester unchanged.

A mixture of 16 g of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dipropyl phosphite, 40 ml of absolute ethanol, and 15.3 g of freshly prepared silver oxalate was prepared in the above-described apparatus. The mixture was stirred in the dark at 80° for six hours. The precipitate was removed and alcohol was distilled off; we recovered 12.4 g of unchanged 2-(2-chloroethoxy)-1-(chloromethyl)ethyl dipropyl phosphite.

Action of Acetyl Chloride on Cyclic Alkylene 2-(2-Chloroethoxy)-1-(chloromethyl)ethyl Phosphites. 6.8 g of acetyl chloride was added dropwise to 23 g of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl (chloromethyl)ethylene phosphite in an Arbuzov flask. The temperature rose by 6°. The mixture was kept at 32° for one hour and then at 55° for 30 minutes. By distillation of the reaction product we isolated 3.1 g (24%) of (chloromethyl) ethylene phosphorochloridite; b.p. 72-72.5° (10 mm); d_4^{20} 1.4810; n_D^{20} 1.5100. Found: C 21.06; H 3.11; Cl 39.94; P 17.26%; MR 35.33. $C_3H_5O_2Cl_2P$. Calculated: C 20.60; H 2.88; Cl 40.54; P 17.71%; MR 35.43. This acid chloride reacted vigorously with water and gave (chloromethyl)ethylene hydrogen phosphite; b.p. 74° (0.012 mm); n_D^{20} 1.4930.

We also isolated 4.8 g (20.8%) of unchanged 2-(2-chloroethoxy)-1-(chloromethyl)ethyl (chloromethyl)ethylene phosphite; b.p. 134-135° (0.18 mm); d_4^{20} 1.3890; n_D^{20} 1.5000 (Table 1, No. 11). The residue (9.2 g) distilled with decomposition over a wide range of temperature; on redistillation of the distillate we were unable to isolate a definite product. In the flask there remained 0.8 g (3.5%) of a colorless viscous liquid, which in constants and analysis corresponded to the product of the isomerization of 2-(2-chloroethoxy)-1-(chloromethyl)ethyl (chloromethyl)ethylene phosphite (Table 2, No. 11). We did not succeed in isolating any 2-(2-chloroethoxy)-1-(chloromethyl)ethyl acetate

[1-chloro-3-(2-chloroethoxy)2-propanol acetic ester]. A sample of this acetic ester was prepared by the reaction of acetyl chloride with 1-chloro-3-(2-chloroethoxy)-2-propanol in dry ether in presence of triethylamine; b.p. 122-123° (10 mm); d_4^{20} 1.2420; n_D^{20} 1.4638; found, MR 47.76. $C_7H_{12}O_3Cl_2$. Calculated, MR 47.56.

SUMMARY

1. On vacuum distillation dialkyl 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites undergo redistribution of phosphorus-attached alkoxyls.

2. When heated, mixed 2-(2-chloroethoxy)-1-(chloromethyl)ethyl phosphites not only undergo the main, isomerization reaction, but also react with elimination of alkyl chloride.

3. The action of acetyl chloride on 2-(2-chloroethoxy)-1-(chloromethyl)ethyl (chloromethyl)ethylene phosphite leads to the formation of (chloromethyl)ethylene phosphorochloridite.

LITERATURE CITED

1. M. I. Kabachnik and P. A. Rossiiskaya, Izv. AN SSSR. Ord. khim. n. 95 (1948).
2. A. N. Pudovik and B. E. Ivanov, Izv. AN SSSR. Otd. khim. n. 947 (1952).
3. V. K. Khairullin, A. I. Ledeneva, and V. S. Abramov, Zh. obshch. khimii 29, 2355 (1959).
4. V. S. Abramov and V. K. Khairullin, Zh. obshch. khimii 27, 444, 1365, 2381 (1957); Trudy Kazanskogo khimiko-tekhnologicheskogo inst. im. S. M. Kirova, No. 23, 77 (1957).
5. E. Fourneau and J. Ribas, Zbl. 896 (1927).
6. A. E. Arbuzov, Structure of Phosphorous Acids and Their Derivatives [in Russian]. Dissertation, St. Petersburg (1905).
7. M. I. Kabachnik, Izv. AN SSSR. Otd. khim. n. 403 (1946).
8. M. I. Kabachnik, Izv. AN SSSR. Otd. khim. n. 631 (1947).
9. N. I. Rizpolozhenskii and A. A. Muslinkin, Izv. AN SSSR. Otd. khim. n. 1600 (1961).
10. A. N. Pudovik and É. M. Faizullin, Zh. obshch. khimii 32, 231 (1962).
11. A. E. Arbuzov, V. M. Zoroastrova, and N. I. Rizpolozhenskii, Izv. AN SSSR. Otd. khim. n. 209 (1948); A. E. Arbuzov and V. M. Zoroastrova, Izv. AN SSSR. Otd. khim. n. 779 (1952).
12. B. A. Arbuzov and O. D. Samoilova, Izv. AN SSSR. Otd. khim. n. 717 (1951).
13. Gil'm Kamai and N. A. Chadaeva, Dokl. AN SSSR 45, 81 (1954).
