PRODUCTION OF PHOSPHORYLATED MERCAPTALS OF CHLORAL

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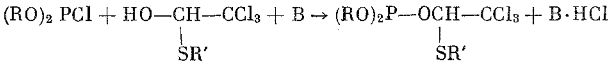
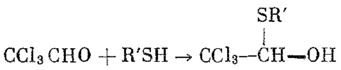
During our research on organophosphorus derivatives of chloral, for use in syntheses of new physiologically active compounds, we have produced, by reacting hemiacetals of chloral with tri- and pentavalent phosphorus acid chlorides, a number of dialkyl 1-alkoxy-2,2,2-trichloroethyl phosphites and phosphates, and investigated some of their properties [1-3]. In continuation of this work, we have now investigated reactions of hemimercaptals of chloral with dialkyl phosphorous acid chlorides in the presence of bases, and produced the corresponding phosphites:



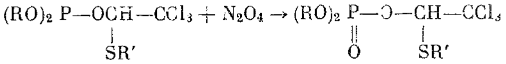
$$(RO)_2PCl + HO-\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3 + B \rightarrow (RO)_2P-O\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3 + B\cdot HCl$$

The hemimercaptals of chloral were prepared by reacting chloral with mercaptans in an inert solvent (with cooling):



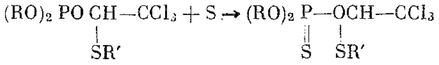
$$CCl_3CHO + R'SH \rightarrow CCl_3-\overset{\displaystyle SR'}{\overset{|}{CH}}-OH$$

These compounds are crystalline, thermally unstable, smelling like mercaptans. When the phosphites are oxidized with nitrogen oxides, the corresponding phosphates are obtained in high yields:



$$(RO)_2P-O\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3 + N_2O_4 \rightarrow (RO)_2\underset{\displaystyle O}{\underset{\|}{P}}-O-\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3$$

We were unable to directly produce these phosphates by reacting hemimercaptals of chloral with dialkyl phosphoric acid chlorides. The phosphites react with elemental sulfur forming the corresponding thiophosphates:



$$(RO)_2PO\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3 + S \rightarrow (RO)_2\underset{\displaystyle S}{\underset{\|}{P}}-O\underset{\displaystyle SR'}{\underset{|}{CH}}-CCl_3$$

TABLE 1

Compound	Yield, %	mp, °C	$\frac{\text{Found}}{\text{Calculated}}$, %			
			C	H	S	Cl
$CCl_3-\underset{\displaystyle OH}{\underset{|}{CH}}-SC_2H$	66,6	69–70	—	—	$\frac{14,70}{15,27}$	$\frac{49,78}{50,84}$
$CCl_3-\underset{\displaystyle OH}{\underset{|}{CH}}-SC_3H_7$	74,7	47–48	$\frac{26,88}{26,84}$	$\frac{4,08}{4,02}$	$\frac{14,11}{14,31}$	$\frac{47,75}{47,65}$
$CCl_3-\underset{\displaystyle OH}{\underset{|}{CH}}-SC_4H_9$	80,8	57–58	—	—	$\frac{13,46}{13,47}$	$\frac{44,75}{44,84}$

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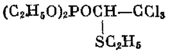
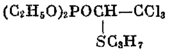
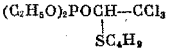
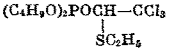
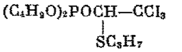
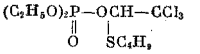
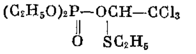
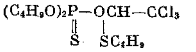
TABLE 2

Compound	Yield, %	Bp, °C (p, mm Hg)	n_D^{20}	d_4^{20}	Found/Calculated, %			
					MR	P, %	Cl, %	S, %
 $(C_2H_5O)_2POCH(SC_2H_5)-CCl_3$	53,1	88—90 (0,03)	1,4965	1,2821	75,13 74,81	9,21 9,40	32,55 32,32	9,91 9,71
 $(C_2H_5O)_2POCH(SC_3H_7)-CCl_3$	59,6	89 (0,03)	1,4900	1,2494	79,48 79,43	9,66 9,02	30,37 31,00	9,88 9,31
 $(C_2H_5O)_2POCH(SC_4H_9)-CCl_3$	57,4	97—99 (0,025)	1,4930	1,2302	84,45 84,05	8,60 8,67	30,20 29,79	9,24 8,95
 $(C_4H_9O)_2POCH(SC_2H_5)-CCl_3$	12,6	107—110 (0,03)	1,4840	1,1875	92,88 93,28	8,06 8,04	26,60 27,62	—
 $(C_4H_9O)_2POCH(SC_3H_7)-CCl_3$	36,0	115—117 (0,03)	1,4870	1,1772	97,60 97,90	7,93 7,75	26,48 26,65	
 $(C_4H_9O)_2POCH(SC_4H_9)-CCl_3$	43,2	132—135 (0,035)	1,4860	1,1563	102,67 102,52	7,57 7,49	25,50 25,75	—
 $(C_2H_5O)_2P(=O)-OCH(SC_4H_9)-CCl_3$	65,4	111—112 (0,02)	1,4815	1,2822	82,93 82,97	8,43 8,29	28,17 28,51	—
 $(C_2H_5O)_2P(=O)-OCH(SC_2H_5)-CCl_3$	61,0	113—114 (0,03)	1,4840	1,3408	73,72 73,74	9,41 8,97	31,07 30,82	
 $(C_4H_9O)_2P(=S)-OCH(SC_4H_9)-CCl_3$	43,5	145—148 (0,03)	1,4993	1,1958	109,44 108,93	7,35 6,96	—	14,39 14,37

The IR spectra of the compounds obtained do not disagree with the proposed structure.

EXPERIMENTAL

Production of Hemimercaptals of Chloral

2,2,2-Trichloro-1-hydroxyethyl Ethyl Sulfide. Into a four-necked flask with stirrer were charged 31 g of ethyl mercaptan and 150 ml of ether. Then 73.7 g of chloral were added dropwise, with stirring and cooling. Subsequently, the temperature was allowed to rise to room temperature, and the ether was evaporated under vacuum. The crystalline product was recrystallized from petroleum ether; the yield was 70 g (66.6%); mp 69-70°C.

2,2,2-Trichloro-1-hydroxyethyl Propyl Sulfide and 2,2,2-Trichloro-1-hydroxyethyl Butyl Sulfide. These were produced analogously.

Constants of these compounds and analytical results are given in Table 1.

Production of 2,2,2-Trichloro-1-thioalkylethyl Dialkyl Phosphites

2,2,2-Trichloro-1-thioethylethyl Diethyl Phosphite. Into a four-necked flask with stirrer were charged 20.9 g of 2,2,2-trichloro-1-hydroxyethyl ethyl sulfide, 10.1 g of $(C_2H_5)_3N$ and 250 ml of ether. The mixture was cooled to 10-15°C, and 15.6 g of diethyl phosphorous acid chloride were added dropwise. $(C_2H_5)_3N\cdot HCl$ was precipitated. The mixture was left overnight to complete the reaction, and then the precipitate was filtered off, the ether was evaporated, and the residue was distilled under vacuum. After two distillations, a product boiling at 88-90° (0.03 mm) was obtained.

In an analogous way were obtained other 2,2,2-trichloro-1-thioalkylethyl dialkyl phosphites, whose constants are given in Table 2.

Production of 2,2,2-Trichloro-1-thioalkylethyl Dialkyl Phosphates

These compounds were produced by oxidizing the corresponding phosphites with nitrogen oxides, as described in [4]. Constants of these compounds are given in Table 2.

Production of 2,2,2-Trichloro-1-thiobutylethyl Dibutyl Thiophosphate

Into a flask with reflux condenser were charged 8.6 g of 2,2,2-trichloro-1-thiobutylethyl dibutyl phosphite and 0.7 g of elemental sulfur. The mixture was heated; the incorporation of sulfur into the phosphite occurred at 90-120°. After two distillations under vacuum, 4 g (43.5%) of the product were obtained; bp 145-147°C (0.03 mm). Constants are given in Table 2.

CONCLUSIONS

By reaction between dialkyl phosphorous acid chlorides and 2,2,2-trichloro-1-hydroxyethyl alkyl sulfides (hemimercaptals of chloral) the corresponding phosphites were obtained. These phosphites can be oxidized to phosphates; they react with sulfur forming the corresponding thiophosphates.

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3. K. V. Nikonorov, É. A. Gurylev, and A. V. Chernova, Izv. Akad. Nauk SSSR, Ser. Khim., 587 (1968).
4. J. R. Cox and F. M. Westheimer, J. Am. Chem. Soc., 80, 5441 (1958).