Synthesis and physicochemical properties of *O*-haloalkyl *O*-(alkyl, aryl) chlorothiophosphates and *O*-haloalkyl chloro(alkyl, dialkylamido)thiophosphates

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Synthesis of *O*-haloalkyl *O*-(alkyl, aryl) chlorothiophosphates and *O*-haloalkyl chloro(alkyl, dialkylamido)thiophosphates is described. Interpretation of infrared, ultraviolet, and ^{31}P NMR spectra is given.

Описано получение *O*-галоалкил *O*-(алкил, арил) хлоротиофосфатов и *O*-галоалкил хлоро(алкил, диалкиламидо)тиофосфатов. Приводится интерпретация инфракрасных, ультрафиолетовых и ^{31}P ЯМР спектров полученных соединений.

It is generally known that esters of chlorothiophosphoric acid usually exhibit various biocidal properties and are mainly used as starting compounds in the synthesis of other organophosphoric compounds. In the literature methods of preparation of *O*-(2-fluoroethyl) *O*-ethyl chlorothiophosphate [1] and of *O*-(2-fluoroethyl) *O*-alkyl chlorothiophosphates [2] as well as of *O*-chloroalkyl *S*-alkyl(aryl, arylalkyl) chlorothiophosphates [3] and of *S*-chloroethyl chloro(dialkylamido)dithiophosphates [4] are described.

As it is known that the thiophosphoric group attached to the various types of organic compounds causes their interesting biocidal properties, novel esters of chlorothiophosphoric acid were synthesized, which were used in the synthesis of 5-pyridazinyl thiophosphates published previously [5].

Experimental

Infrared spectra of compounds prepared were recorded with a UR 20 (Zeiss, Jena) instrument in trichloromethane and tetrachloromethane ($c = 0.10$—0.15 mol dm^{-3}, cell thickness 0.113 mm), the wavenumber calibration was checked against the spectrum of polystyrene. Ultraviolet spectra were recorded with a Specord UV VIS (Zeiss, Jena) instrument in methanol ($c = 2 \times 10^{-5}$—5×10^{-5} mol dm^{-3}, cell thickness 10 mm).

^{31}P NMR spectra were recorded with an FX-60 Jeol instrument (40.26 MHz) in C^2HCl_3 using H_3PO_4 (85 %) as external standard. Assignment of the signals was made by a comparison with those of compounds with similar structures described in the literature [6, 7].

The purity of compounds was verified by means of thin-layer chromatography on Silufol R (Lachema, Brno) using toluene as a developing agent. Detection was carried out by means of 0.5 % solution of 2,6-dibromoquinone-4-chloroimide in petroleum ether at 120 °C. Compounds were purified by distillation under reduced pressure.

O-Haloalkyl O-alkyl chlorothiophosphates

Procedure A (VI—VIII, XIII, XIV, XVII)

To *O*-haloalkyl dichlorothiophosphate (0.1 mol) in toluene (60 cm^3) potassium alcoholate (0.105 mol) in toluene (50 cm^3) was added over a period of 0.5 h with stirring at the reaction temperature of 0—8 °C. Stirring was continued for 3 h at room temperature. The course of the reaction was monitored by TLC. After completion of the reaction the reaction mixture was washed with ice cold water (3×50 cm^3). The toluene layer was separated, dried with anhydrous $CaCl_2$ and toluene was distilled off. The residue was purified by distillation under reduced pressure.

Procedure B (I—III, V, XV—XVIII, XXIV)

To *O*-haloalkyl dichlorothiophosphate (0.2 mol) and *S*-haloalkyl dichlorothiophosphate (0.2 mol), respectively, in toluene (100 cm^3) and cyclohexane, respectively, a mixture of the appropriate alcohol (0.21 mol) and triethylamine (0.21 mol) is added over a period of 1 h at 5—10 °C. After addition the reaction mixture was stirred for 2—5 h at room temperature. Monitoring the reaction and the treatment of the reaction mixture was carried out as by procedure *A*.

Procedure C (IV, VI, XIII)

To *O*-alkyl dichlorothiophosphate (0.1 mol) in benzene (60 cm^3) a mixture of 2-chloroethanol and 3-chloropropanol (0.105 mol), respectively, and triethylamine (0.105 mol) or pyridine in benzene was gradually added with efficient stirring at 5—10 °C. After completion of the addition the reaction mixture was stirred for 3—6 h and the course of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was treated as by procedure *A*.

O-Haloalkyl chloro(alkyl, dialkylamido)thiophosphates (X—XII)

To *O*-haloalkyl dichlorothiophosphate (0.5 mol) in toluene (200 cm^3) the appropriate amine (1.05 mol) in toluene (50 cm^3) was added over a period of 1 h with efficient stirring

at −5—5 °C and then the reaction mixture was stirred at 20—30 °C until the reaction of starting compounds was completed. The treatment of the reaction mixture was carried out as by procedure *A*.

O-Haloalkyl O-aryl chlorothiophosphates (*IX*, *XIX—XXIII*)

To *O*-haloalkyl dichlorothiophosphate (0.2 mol) in toluene (100 cm^3) a mixture, prepared by solving potassium or sodium hydroxide (0.21 mol) and an appropriate phenol (0.21 mol) in water (70 cm^3), was added with efficient stirring over a period of 1 h at room temperature. After addition the reaction mixture was stirred for 3 h at 40—60 °C. The course of the reaction was monitored by TLC on silufol plates. After the reaction was complete, the reaction mixture was cooled, the organic layer was separated and treated as by procedure *A*.

Discussion

A series of *O*-haloalkyl *O*-(alkyl, aryl) chlorothiophosphates and *O*-haloalkyl chloro(alkyl, dialkylamido)thiophosphates has been synthesized. Their structure was proved by spectral methods. Characterization of chlorothiophosphates is presented in Table 1.

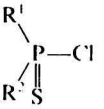
A substantial part of esters of chlorothiophosphoric acid was prepared by the reaction of *O*-(2-chloroethyl) dichlorothiophosphate with alcohol, alkaline alcoholate, amine, and phenol. By monitoring the course of the reaction it was found that the substitution of the chlorine atom attached to the phosphorus atom proceeded with difficulties with increasing sterical hindrances of the nucleophilic reactants. In these reactions alcohols having the C_1—C_5 carbon chain were used whereby the chain length had a smaller influence on the reaction course than its branching.

The attempts to prepare *O*-(2-chloroethyl) *O*-*tert*-butyl chlorothiophosphate were unsuccessful. It can be assumed that steric hindrances are responsible for the unsuccessful preparation. The reactions were carried out with efficient stirring at the temperature of the reaction mixture $\theta = -5$ °C to 15 °C and the reaction time varied from 2 h to 8 h.

By studying the course of the reactions it was found that the course of nucleophilic substitution was significantly dependent on temperature. Therefore, it was convenient during the addition of the nucleophilic agent to maintain the temperature of the reaction mixture at −5 °C to 25 °C and then to stirr the reaction mixture at 15 °C to 60 °C. Higher temperatures facilitated the course of concurrent reactions by which mainly thiophosphates were formed.

Table I

Physicochemical characteristics of the prepared compounds



Compound	R^1	R^2	Formula M_r	w_i(calc.)/% w_i(found)/%			Yield	B. p./°C p/Pa
				P	S	Cl	%	
I	$ClCH_2CH_2O$	CH_3O	$C_3H_7Cl_2O_2PS$	14.82	15.34	33.93	85.4	65
			208.96	14.42	15.98	33.44		13.3
II	$ClCH_2CH_2O$	C_2H_5O	$C_4H_9Cl_2O_2PS$	13.88	14.31	31.80	77.4	76 78
			222.97	14.10	14.62	31.66		26.6
III	$ClCH_2CH_2O$	C_3H_7O	$C_5H_{11}Cl_2O_2PS$	13.06	13.49	29.91	73.7	82 86
			236.98	13.18	13.93	30.48		13.3
IV	$ClCH_2CH_2O$	i-C_3H_7O	$C_5H_{11}Cl_2O_2PS$	13.06	13.49	29.91	64.0	68 72
			236.98	13.22	13.62	30.16		6.65
V	$ClCH_2CH_2O$	C_4H_9O	$C_6H_{13}Cl_2O_2PS$	12.34	12.77	28.24	62.7	82 87
			250.99	12.01	12.58	28.71		26.7
VI	$ClCH_2CH_2O$	i-C_4H_9O	$C_6H_{13}Cl_2O_2PS$	12.34	12.77	28.24	86.5	76 79
			250.99	12.11	12.99	28.48		26.6
VII	$ClCH_2CH_2O$	-C_4H_9O	$C_6H_{13}Cl_2O_2PS$	12.34	12.77	28.24	81.4	81 85
			250.99	13.05	12.84	28.21		13.3
VIII	$ClCH_2CH_2O$	i-$C_5H_{11}O$	$C_7H_{15}Cl_2O_2PS$	11.68	12.09	26.85	74.3	85 88
			265.00	11.28	12.84	25.59		6.7
IX	$ClCH_2CH_2O$	C_6H_5O	$C_8H_9Cl_2O_2PS$	11.42	11.83	26.15	70.1	97 100
			271.01	11.50	12.26	26.41		6.3
X	$ClCH_2CH_2O$	i-C_4H_9NH	$C_6H_{14}Cl_2NOPS$	12.38	12.82	28.35	88.8	108 110
			249.99	12.82	13.01	28.78		26.6
XI	$ClCH_2CH_2O$	C_4H_9NH	$C_6H_{14}Cl_2NOPS$	12.38	12.82	28.35	85.4	112 114
			249.99	12.45	13.62	28.50		26.6

Table 1 (Continued)

Compound	R^1	R^2	Formula M_r	w_i(calc.)/% w_i(found)/%			Yield	B. p./°C p/Pa
				P	S	Cl	%	
XII	$ClCH_2CH_2O$	$(C_2H_5)_2N$	$C_6H_{14}Cl_2NOPS$	12.38	12.82	28.35	87.4	92—95
			249.99	12.35	12.67	28.62		6.7
XIII	$ClCH_2CH_2CH_2O$	i-C_4H_9O	$C_7H_{15}Cl_2O_2PS$	11.68	12.09	26.74	70.9	110—114
			265.00	11.13	12.11	26.77		66.5
XIV	$ClCH_2CH(CH_3)O$	i-C_4H_9O	$C_7H_{15}Cl_2O_2PS$	11.68	12.09	26.74	73.6	90—93
			265.00	11.93	12.29	26.50		53.2
XV	FCH_2CH_2O	i-C_4H_9O	$C_6H_{13}FClO_2PS$	13.20	13.66	15.11	76.5	75—77
			234.54	13.90	13.15	15.67		33.3
XVI	FCH_2CH_2O	C_2H_5O	$C_4H_9FClO_2PS$	14.99	15.52	17.16	71.0	50—52
			206.52	15.08	15.87	17.43		26.6
XVII	FCH_2CH_2O	C_3H_7O	$C_5H_{11}FClO_2PS$	14.03	14.53	16.07	65.4	55—58
			220.54	14.38	15.01	16.59		13.3
XVIII	$BrCH_2CH_2O$	i-C_4H_9O	$C_6H_{13}BrClO_2PS$	10.41	10.85	11.99	73.9	95—99
			295.45	10.50	10.80	12.62		66.5
XIX	$ClCH_2CH_2O$	*m*-F—C_6H_4O	$C_8H_8FCl_2O_2PS$	10.71	11.03	24.53	68.1	120—125
			289.01	10.69	11.07	23.88		26.6
XX	$ClCH_2CH_2O$	*p*-Br—C_6H_4O	$C_8H_8BrCl_2O_2PS$	8.85	9.16	20.26	72.9	150—153
			349.91	8.25	9.55	20.95		26.6
XXI	$ClCH_2CH_2O$	*p*-CH_3S—C_6H_4O	$C_9H_{11}Cl_2O_2PS_2$	9.76	20.22	22.36	58.8	*
			317.08	10.20	20.13	21.99		
XXII	$ClCH_2CH_2O$	3,5-$(CH_3)_2$—C_6H_3O	$C_{10}H_{13}Cl_2O_2PS$	10.35	10.72	23.70	63.5	140—143
			299.03	10.24	11.39	24.01		13.3
XXIII	$ClCH_2CH_2O$	3-CH_3-4-NO_2—C_6H_3O	$C_9H_{10}Cl_2NO_4PS$	9.38	9.71	21.48	30.0	*
			330.02	9.77	10.02	21.63		
XXIV	$ClCH_2CH_2S$	C_3H_7O	$C_5H_{11}Cl_2OPS_2$	12.24	25.34	28.02	41.0	100—105
			253.04	12.67	25.12	28.75		53.2

* Compounds being decomposed at boiling point, they were purified by column chromatography on SiO_2 using toluene as eluent.

Table 2

Spectral characteristics of the prepared compounds

Compound	$\tilde{\nu}$/cm^{-1}			λ_{max}/nm log (ε/(m^2 mol^{-1}))	^{31}P NMR δ/ppm
	ν(P—Cl)	ν(P=S)	ν(P—O—C)		
I	499	655 727	1028	212.5	70.42
	494	658 702	1026	3.193	
II	500	659 694	1020	211.5	68.3
	498	656 716	1026	3.282	
III	506	656 705	1005	208.0	68.0
	504	657 718	1006	2.681	
IV	514	658 697	1000	212.5	68.2
	503	657 702	1001	3.200	
V	507	655 694	1019	213.5	68.4
	498	655 698	1016	3.281	
VI	507	657 723	1015	213.0	68.5
	512	668 731	1017	3.309	
VII	508	655 705	992	212.0	67.6
	515	667 732	1003	3.627	
VIII	497	652 697	1002	213.0	68.4
	498	662 723	996	3.139	
IX	510	661 706	1017	211.0	63.4
	508	670 720	1017	3.789	
X	486	657 746	1031	216.5	72.7
	488	673 744	1031	3.350	
XI	481	655 701	1023	212.0	72.6
	491	655 730	1036	3.636	
XII	469	628 704	1018	212.0	75.3
	478	637 727	1029	3.666	
XIII	517	662 725	1015	214.5	68.8
	514	679 725	1013	3.390	
XIV	512	664 703	1001	213.0	67.8
	510	663 708	1003	3.310	
XV	534	660 696	1020	212.5	69.2
	529	668 726	1018	3.241	
XVIII	503	666 719	1023	210.0	—
	505	671 730	1025	3.222	
XIX	506	655 714	1008	214.0	68.3
	502	656 725	1009	3.258	
XX	516	676 724	1014	214.0	—
	516	677 729	1014	3.341	
XXI	509	673 713	1004	210.5	—
	511	679 740	1010	3.191	

By the preparation of chlorothiophosphates the content of water in alcohols used and also the way of addition of reaction components played an important role. By the preparation of *O*-haloalkyl *O*-alkyl chlorothiophosphates the use of alcohol and triethylamine instead of the alkaline alcoholate was very convenient as a laborious preparation of the appropriate potassium or sodium alcoholate containing a larger number of carbon atoms was excluded. Moreover, a difficult addition of alcoholates and a total treatment with them was also excluded. The mentioned change of nucleophilic agent had practically no influence on the yield and the purity of product. By the preparation of *O*-haloalkyl chloro(alkyl, dialkylamido)thiophosphates an appropriate amine used in twofold molar amount acted simultaneously as a nucleophilic reactant.

O-Haloalkyl *O*-(X-phenyl) chlorothiophosphates were prepared in such a way that an aqueous solution of the alkaline hydroxide and the appropriate phenol was gradually added to *O*-haloalkyl dichlorothiophosphate in organic solvent, *e.g.* toluene, at 20 °C to 25 °C and the efficient stirring of the reaction mixture was necessary as a two-phase system was formed.

Spectral characteristics of compounds prepared are listed in Table 2.

The ν(P—Cl) bands are in the region of $\tilde{\nu} = 490—517\ \mathrm{cm}^{-1}$ (in trichloromethane). On passing from trichloromethane to tetrachloromethane a significant wavenumber shift is not observed. Higher values of the ν(P—Cl) were observed only with compound *XV* where R^1 represents 2-fluoroethoxy group. The ν(P=S) bands are observed in the region of $\tilde{\nu} = 650—730\ \mathrm{cm}^{-1}$ whereby the influence of substituents on their values is negligible. The wavenumbers of the ν(P—O—C_{aliph}) bands are relatively constant and it seems that they are not influenced by the nature of the hydrocarbon chain.

In the ultraviolet spectra of compounds studied the bands in the region of $\lambda = 208—216$ nm are observed and the λ_{max} of these bands is only slightly influenced by the nature of the substituents. The ^{31}P NMR spectra of compounds studied indicate that the length of the hydrocarbon chain does not influence significantly the chemical shift of the phosphorus atom. The higher values of chemical shifts were observed in the spectra of compounds *X*—*XII* containing the alkylamido or dialkylamido groups.

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