Synthesis and pesticidal activity of *O*,*O*-dialkyl *O*-(5-chloro--1-alkyl-6-oxo-1*H*-pyridazin-4-yl) thiophosphates

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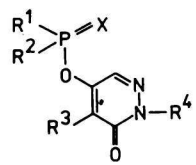
O,*O*-Dialkyl *O*-(5-chloro-1-methyl-6-oxo-1*H*-pyridazin-4-yl) and *O*-ethyl *O*-isopropyl *O*-(5-chloro-1-alkyl-6-oxo-1*H*-pyridazin-4-yl) thiophosphates were synthesized and tested for contact and systemic insecticidal, acaricidal, and ovicidal activities and also as soil insecticides on model organisms. The highest activity was observed with *O*-ethyl *O*-isopropyl *O*-(5-chloro-1-methyl-6-oxo-1*H*-pyridazin-4-yl) thiophosphate.

Описывается синтез *O*,*O*-диалкил *O*-(5-хлор-1-метил-6-оксо-1*H*-пиридазин-4-ил) и *O*-этил *O*-изопропил *O*-(5-хлор-1-алкил-6-оксо-1*H*-пиридазин-4-ил) эфиров тиофосфорной кислоты. Приготовленные соединения были испытаны на контактное и системное инсектицидное, акарицидное и овицидное действие, а также по действию на модельные организмы как почвенные инсектициды. Самое сильное действие было обнаружено в случае *O*-этил *O*-изопропил *O*-(5-хлор-1-метил-6-оксо-1*H*-пиридазин--4-ил) тиофосфата.

Studies on pesticidal activities of the so far synthesized 4-pyridazinyl organophosphates of the formula *A*

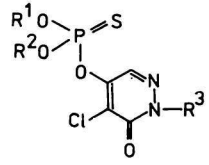


A

revealed that most compounds were active in tests for contact insecticidal activity on *Aphis fabae* SCOP and acaricidal activity on females of *Tetranychus urticae* KOCH. Fewer compounds were highly active in tests for contact and time activities on *Musca domestica* L., contact insecticidal activity on *Calandra granaria* L., and ovicidal activity on eggs of *T. urticae*.

The most active compounds were those with R^1 = alkoxy, R^2 = alkoxy, *N*-alkylamido, ethyl, phenyl, R^3 = alkoxy, chlorine, hydrogen, R^4 = alkyl, benzyl, phenyl, and X = sulfur. They were especially active when R^1 = ethoxy, R^2 = isopropoxy, R^3 = methoxy. *O*-Ethyl *O*-isopropyl *O*-(5-methoxy-1-methyl-6-oxo-1*H*-pyridazin-4-yl) thiophosphate (Pyridathion) as soil insecticide was studied in detail. The structure of this compound and its toxicity on haematothermal organisms were studied simultaneously.

Continuing the studies of 4-pyridazinyl organophosphates, we focused our attention on the synthesis of the compounds of the formula *B*.



B

With these compounds we investigated the effect of the substituents R^1 and R^2 on pesticidal activity when R^3 = methyl as well as the effect of R^3 on pesticidal activity when R^1 = ethyl and R^2 = isopropyl.

The synthesis was carried out by the reaction of *O*,*O*-dialkyl chlorothiophosphate with sodium or potassium 5-chloro-1-alkyl-6-oxo-1*H*-pyridazin-4-olate in acetonitrile at the boiling temperature of the reaction mixture for 2—6 h. In those cases when the starting *O*,*O*-dialkyl chlorothiophosphate could be distilled with steam (R^1 = methyl, ethyl, R^2 = methyl, isobutyl) the crude product was purified by counter-current distillation with steam. The other compounds were purified by column chromatography. The purity of compounds was checked by t.l.c. (Table 1).

It was found that the synthesized compounds did not exhibit contact insecticidal activity on *C. granaria* and systemic activity on *A. fabae* in 0.01 and 0.1% concentrations. Relatively low activity values were obtained in tests on *M. domestica* for contact insecticidal activity, however, the activity on *A. fabae* was essentially higher. The compounds *V*, *VII*, and *X* were orderly on the level with the used standard Fenitrothion. The compounds were highly active on females of *T. urticae;* the compound *V* was orderly on the level with the standard Karbofenthion. On the other hand, the ovicidal activities of the compounds tested were low (Table 2).

The effect of the synthesized compounds on soil parasites was investigated on model organisms (larvae of *M. domestica* and *Tenebrio molitor* L.). The compounds *III*, *V*, *VII*, and *X* showed in 24 p.p.m. concentration 20% activity on *M. domestica,* while the compounds *IV*, *V*, and *XIV* exhibit 60% activity on *T. molitor* in the same concentration. The compound *V* will be subjected to detailed investigation in experiments against soil parasites.

Table 1

Characterization of the synthesized compounds

Compound	R^1	R^2	R^3	Formula	M	Calculated/found			Yield %	n_D^{20}
						% P	% S	% Cl		
I	CH_3	CH_3	CH_3	$C_7H_{10}ClN_2O_4PS$	284.64	10.88	11.26	12.46	81.1	1.5527
						10.96	11.41	12.38		
II	CH_3	C_2H_5	CH_3	$C_8H_{12}ClN_2O_4PS$	298.66	10.37	10.73	12.03	78.8	1.5441
						10.30	10.81	12.21		
III	C_2H_5	C_2H_5	CH_3	$C_9H_{14}ClN_2O_4PS$	312.69	9.91	10.23	11.34	86.2	1.5362
						9.65	10.58	11.68		
IV	C_2H_5	C_3H_7	CH_3	$C_{10}H_{16}ClN_2O_4PS$	326.70	9.49	9.78	10.85	87.7	1.5318
						9.34	10.06	10.91		
V	C_2H_5	$(CH_3)_2CH$	CH_3	$C_{10}H_{16}ClN_2O_4PS$	326.70	9.49	9.78	10.85	81.9	1.5211
						9.52	9.92	11.01		
VI	C_3H_7	C_3H_7	CH_3	$C_{11}H_{18}ClN_2O_4PS$	340.72	9.09	9.41	10.41	89.2	1.5242
						9.16	9.52	10.35		
VII	$(CH_3)_2CH$	$(CH_3)_2CH$	CH_3	$C_{11}H_{18}ClN_2O_4PS$	340.72	9.09	9.41	10.41	81.1	1.5220
						9.22	9.49	10.60		
VIII	$(CH_3)_2CH$	$(CH_3)_2CHCH_2$	CH_3	$C_{12}H_{20}ClN_2O_4PS$	354.74	8.73	9.04	9.99	92.6	1.5198
						8.86	9.12	10.11		
IX	$(CH_3)_2CHCH_2$	$(CH_3)_2CHCH_2$	CH_3	$C_{13}H_{22}ClN_2O_4PS$	368.76	8.40	8.69	9.62	90.2	1.5160
						8.36	8.81	9.80		

Table 1 (Continued)

Compound	R^1	R^2	R^3	Formula	M	Calculated/found			Yield %	n_D^{20}
						% P	% S	% Cl		
X	C_2H_5	$(CH_3)_2CH$	C_2H_5	$C_{11}H_{18}ClN_2O_4PS$	340.72	9.09 9.28	9.41 9.31	10.41 10.55	88.2	1.5198
XI	C_2H_5	$(CH_3)_2CH$	C_3H_7	$C_{12}H_{20}ClN_2O_4PS$	354.74	8.73 8.82	9.04 9.19	9.99 10.21	79.8	1.5168
XII	C_2H_5	$(CH_3)_2CH$	C_4H_9	$C_{13}H_{22}ClN_2O_4PS$	368.76	8.40 8.61	8.69 8.58	9.62 9.49	90.2	1.5175
XIII	C_2H_5	$(CH_3)_2CH$	C_5H_{11}	$C_{14}H_{24}ClN_2O_4PS$	382.79	8.09 8.19	8.38 8.48	9.26 9.19	80.6	1.5150
XIV	C_2H_5	$(CH_3)_2CH$	C_6H_{13}	$C_{15}H_{26}ClN_2O_4PS$	396.81	7.80 8.01	8.10 8.22	8.94 8.80	86.2	1.5130
XV	C_2H_5	$(CH_3)_2CH$	C_6H_{11}	$C_{15}H_{22}ClN_2O_4PS$	394.80	7.84 8.02	8.12 8.26	8.98 9.06	82.6	1.5340
XVI	C_2H_5	$(CH_3)_2CH$	C_6H_5	$C_{15}H_{16}ClN_2O_4PS$	388.75	7.97 8.16	8.25 8.31	9.12 9.09	90.6	*a*
XVII	C_2H_5	$(CH_3)_2CH$	$CH_2—C_6H_5$	$C_{16}H_{18}ClN_2O_4PS$	402.77	7.69 7.60	7.96 8.06	8.80 8.98	78.4	1.5573
XVIII	C_2H_5	$(CH_3)_2CH$	$CH_2—CH=CH_2$	$C_{12}H_{18}ClN_2O_4PS$	352.74	8.78 8.92	9.09 9.18	10.05 10.22	96.2	1.5305

a) Melting point 62—63°C.

Table 2

Insecticidal, acaricidal, and ovicidal activities of the synthesized compounds

Compound	LC_{50} in %			
	Musca domestica	*Aphis fabae*	*Tetranychus urticae*	
			Females	Eggs
I	0.290	0.052	0.048	>0.5
II	>0.5	0.014	>0.1	0.28
III	>0.5	0.0085	0.0046	>0.5
IV	>0.5	0.0092	0.041	0.29
V	>0.5	0.0018	0.0015	>0.5
VI	>0.5	0.043	>0.1	0.31
VII	>0.5	0.0010	>0.1	0.32
VIII	>0.5	0.041	>0.1	0.30
IX	>0.5	0.066	>0.1	0.26
X	0.242	0.00093	0.014	0.221
XI	0.280	>0.1	0.0042	0.274
XII	0.368	0.0022	0.0043	0.208
XIII	0.310	0.042	0.053	0.241
XIV	0.462	0.040	0.038	0.42
XV	>0.5	>0.1	0.031	0.201
XVI	>0.5	0.092	0.015	>0.5
XVII	>0.5	0.041	0.032	0.22
XVIII	>0.5	0.021	0.019	>0.5
Fenitrothion	0.0021	0.00083	—	—
Karbofenthion	—	—	0.00062	0.0012

Experimental

Thin-layer chromatography was performed on Silufol plates (Lachema, Brno) in the systems of benzene or benzene—acetone (9 : 1). Detection was carried out with 0.5% DQC (2,6-dibromo-4-chloroimidoquinone) in petroleum ether at 120°C. Column chromatography was performed on Silica gel 100/160 mesh (Lachema, Brno) activated at 140°C for 6 h before use. Benzene or the mixture of benzene and acetone (acetone added according to the impurities present) was used as eluting agent. The course of separation was followed by t.l.c.

At the purification of the reaction mixture by steam, 20% toluene solution of the sample was added dropwise on top of a column filled with Raschig and with steam passing through the column from below. The volatilizing components (toluene, the unchanged starting chlorothiophosphate, and maybe triesters) with steam were captured in a receiver and the crude product passed through a siphon into a flask. The product was extracted with toluene (2×50 ml) and after drying the solution with anhydrous sodium sulfate, toluene was distilled off under reduced pressure.

Contact insecticidal activity was followed on *Musca domestica* L., *Calandra granaria* L., and *Aphis fabae* SCOP using Fenitrothion (*O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) thiophosphate) as standard. Systemic insecticidal activity was followed on *A. fabae* using Thiometon (*O,O*-dimethyl *S*-(2-ethylthioethyl) dithiophosphate) as standard. Acaricidal activity was followed on females of *Tetranychus urticae* KOCH, ovicidal activity on eggs of *T. urticae* using Karbofenthion (*O,O*-diethyl *S*-(4-chlorophenylthiomethyl) dithiophosphate) as standard. The methods for determinations of insecticidal, acaricidal, and ovicidal activities were published in [1, 2]. The activity against soil parasites was followed on model organisms (larvae of *M. domestica* and *Tenebrio molitor* L.) after the method described in [3].

O,O-Dialkyl O-(1-alkyl-5-chloro-6-oxo-1H-pyridazin-4-yl) thiophosphates

To sodium or potassium 5-chloro-1-alkyl-6-oxo-1*H*-pyridazin-4-olate (0.11 mol) in acetonitrile (120 ml) *O,O*-dialkyl chlorothiophosphate (0.1 mol) was added and the mixture was stirred at the boiling temperature for 2—6 h. After cooling toluene (150 ml) was added and the solution was washed with water, 5% aqueous solution of sodium carbonate, and water. The compounds *I—V*, *X—XVII* were purified by counter-current distillation with steam and the compounds *VI—IX* by column chromatography. Characterization of the synthesized compounds is in Table 1.

References

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