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PHOSPHORUS-CONTAINING ESTERS OF ANABASINE AND PIPERIDINE

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New phosphorus-containing esters of anabasine and piperidine [O,O-dibutyl-S-(piperidinobutyn-2-yl)-thiophosphate and N-β-(O-pentylphenylphosphonyl)-mercaptoethylanabasine] were synthesized. Their potentiating effect in a mixture with carbophos was determined on spider mites.

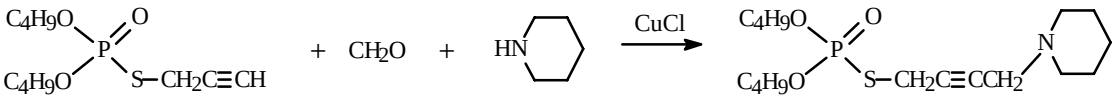
Key words: anabasine, piperidine, phosphorus-containing esters, carbophos, potentiating effect, synergists.

Resistance of spider mites to insectoacaricides is a serious problem for the cotton-growing regions of Uzbekistan.

Some researchers [1, 2] explain the resistance of mites to chemical plant protectors by the activation of metabolic enzymes. It was found that one of the reasons for development of resistance is repeated application of pesticide preparations.

We investigated synergism of O,O-dibutyl-S-(piperidinobutyn-2-yl)-thiophosphate (**1**) and N-β-(O-pentylphenylphosphonyl)-mercaptoethylanabasine (**2**) in a mixture with carbophos on spider mites in a search for effective synergists capable of potentiating their effects in a mixture.

Compound **1** was synthesized using the Mannich reaction:



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The IR spectrum of this compound exhibits absorption bands for the following functional groups (ν, cm^{-1}): 1260 (P=O), 1130 (P–O–C_2H_5), 2240 (–C≡C–), 2850 (C–H).

The PMR spectrum contains signals for two equivalent butyls: multiplets of oxymethylenes (OCH_2) at 3.96 ppm, the splitting of which is due to spin—spin coupling with neighboring methylenes and the P atom. The –CH_2–CH_2– methylenes form a multiplet centered at 1.7 ppm. The terminal methylenes give a triplet at 0.95 ppm. The α-protons of the piperidine ring resonate as a broad triplet at 2.34 ppm (4H, NCH_2); the β- and γ-protons, at 1.2-1.7 ppm (6H, m, CH_2).

The SCH_2 and NCH_2 protons of the bridging group give signals at 3.49 and 3.15 ppm, respectively. The through-space spin—spin couplings of SCH_2–C=C–CH_2N are 2.2 Hz. Furthermore, the S–CH_2 signal is also split into a doublet with J(PH) = 13.5 Hz owing to coupling with the P atom.

The mass spectrum of **1** gives a molecular ion with *m*/*z* 361 (75%), decomposition of which is identical to decomposition of the analogous thiophosphates [3, 4].

N-β-(O-Pentylphenylphosphonyl)-mercaptoethylanabasine was synthesized by the scheme:

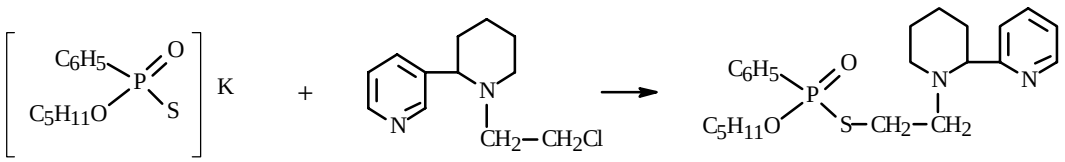

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TABLE 1. Toxicity of Carbophos and Its Mixtures with **1** and **2**

Carbophos conc., %	Mortality, %		
	carbophos	carbophos mixture with **1**	carbophos mixture with **2**
0.01	100	97.4	90.0
0.005	59.1	74.0	80.0
0.001	7.2	80.0	50.0
0.0005	2.9	92.1	25.0
0.0001	0.0	71.2	11.0
0.00001	0.0	78.0	-
LC_{50}	0.004	0.00000006	0.0005

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LC_{50} of **1** = 0.02%; LC_{50} of **2** = 0.05%.

The structure of **2** was confirmed by IR and PMR spectra.

The IR spectrum exhibits characteristic absorption bands (ν, cm^{-1}): 680-700 (–P–S–C–), 1160 (–P–O–C–), 1250 (–P=O), 1450 (–P–C_6H_5), 1370 (–C–CH_3), and 1540 (–N–C in the ring). The PMR spectrum at weak field (7.3-7.8 ppm) has a two-component multiplet of phenyl protons (5H). The α-, α'-, β-, and γ-protons of the pyridine ring are located at 8.34, 8.30, 7.55, and 7.12 ppm. The multiplicity of these signals corresponds to a β-substituted pyridine. The signals of the piperidine ring are distributed as follows: H_{2a} and H_{6a} resonate at 3.04-3.25 ppm; $H_{6a'}$, at 2.15 ppm. Signals of the O-pentyl group are situated as follows: methylene protons of the alcohol OCH_2– appear as a multiplet at 4.52 ppm; of the methylenes (6H, CH_2), as two featureless multiplets at 1.1-1.8 ppm; of the terminal methyl, as a triplet at 0.86 ppm. Signals of S–CH_2–CH_2N form a multiplet at 3.41 ppm and a triplet at 2.2 ppm, respectively.

The mass spectrum of **2** revealed the presence of a molecular ion at *m*/*z* 416, the mass spectrometric fragmentation of which was analogous to decomposition of the molecular ion of O-hexyl-O-(anabasinoisopropyl)phenylphosphonate [5].

Table 1 presents the results from a study of the activity of carbophos (50% emulsified concentrate) and its mixtures with **1** and **2**.

The minimal carbophos concentration capable of killing 100% of the spider mites was 0.01%. Decreasing it by half resulted in the death of 59% of the mites. The population of mites in 24 h after application of 0.0005% carbophos and lower remained at the control level.

A significant increase in mite mortality was observed with use of a mixture of carbophos and **1**. It was found that mite mortality from 0.001% carbophos and 0.05% **1** increased by 11 times; from 0.0005% carbophos and 0.05% **1**, by 32 times compared with pure carbophos. The LC_{50} for spider mites of a composition with various carbophos concentrations and a constant amount of **1** (0.01%) was 0.003%; for **1** (0.005%), 0.001%. Diluting it at a constant concentration of **1** (0.05%) sharply decreases the mite mortality.

The effectiveness of carbophos as its concentration decreases by 10,000 times in the presence of **1** (0.05%) decreases insignificantly, by 20-30%; without **1**, by 10 times and the toxicity of the preparation falls to zero. The average lethal concentration of this composition of preparations for spider mites was 0.00000006%, i.e., 10,000 times greater than LC_{50} for carbophos (0.0045%) and **1** (0.02%) taken separately.

Mite mortality also increases compared with pure carbophos for a mixture of carbophos and **2**. It was found that mite mortality increased by eight times compared with pure carbophos for carbophos (0.0005%) and **2** (0.02%).

Thus, these experiments show the potentiating effect of **1** and **2** in a mixture with carbophos on spider mites. The mixture of carbophos and **1** has the greatest effect. The synergism of **1** and **2** may be due to their ability to suppress the catalytic activity of carboxylesterase [6], which metabolizes hydrolytically carbophos and destroys its toxic properties [2]. Apparently this is an important factor in the development of resistance of spider mites to these insectoacaricides.

EXPERIMENTAL

IR spectra were recorded on a Specord IR-71 instrument in KBr disks; PMR spectra on an XL-200 NMR spectrometer (Varian, USA) at working frequency 200 MHz in CCl_4 or $CDCl_3$. Column chromatography used Al_2O_3 (activity II) with absolute ether eluent.

Mass spectra of **1** and **2** were measured in a MAT-311 instrument (Varian, USA) using a direct probe at ionization-chamber temperature 100-120°C with ionizing potential 70 V, ionizing current 300 μA, and vaporization temperature 20-40°C.

Synthesis of O,O-Dibutyl-S-(piperidinobutyn-2-yl)thiophosphate (1). A mixture of piperidine (1.20 g, 0.014 mol) and paraform (0.64 g, 0.021 mol) in absolute alcohol was boiled for 1-1.5 h, treated with CuCl (0.13 g, 0.0009 mol) and O,O-dibutyl-S-propargylthiophosphate (2.95 g, 0.029 mol) in alcohol, boiled with stirring for 6 h, and treated with HCl (100 mL, 5%). Unreacted reagent was extracted with ether. The aqueous layer was made basic with NH_4OH (25%) and extracted with ether. The ether extracts were dried over anhydrous Na_2SO_4. The solvent was distilled. The final product was purified over a column of Al_2O_3 (activity II, absolute ether eluent). Yield of **1**, 66.0%, $n_D^{20} = 1.4961$.

Synthesis of N-β-(O-Pentylphenylphosphonyl)-mercaptoethylanabasine (2). A mixture of potassium O-pentylphenylthiophosphonate (5.32 g, 0.02 mol) and N-β-chloroethylanabasine (8.90 g, 0.02 mol) in absolute ethanol (100 mL) was refluxed for 4-6 h. The precipitate of KCl was filtered off. Solvent was distilled. The product was purified over Al_2O_3. Yield of **2**, 52%, $n_D^{20} = 1.5226$.

Laboratory populations of *Tetranychus urticae* Koch. were used in the experiments.

The mixture of concentrates was prepared in a 1:1 ratio. The average lethal concentrations causing 50% death of spider mites (LC_{50}) were calculated by least squares methods (Urbakh sample analysis) [7]. For this, freshly cut cotton leaves were placed on a layer of moistened cotton in Petri dishes. A ring of entomological non-dehydrating glue was placed on this. Male mites (25, one application) were transplanted inside the ring. Each experiment was repeated four times. The mites were sprayed after 2 h with the appropriate carbophos dilutions and its mixtures with **1** and **2**; the controls, with water. Mite mortality was calculated taking into account mortality of the controls according to the Abbot formula [8].

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