Synthesis and biological activity of *S*-(*N*′,*N*′-dialkylthiocarbamoyl)(*N*,*N*-dialkylamido)ethyldithiophosphonates

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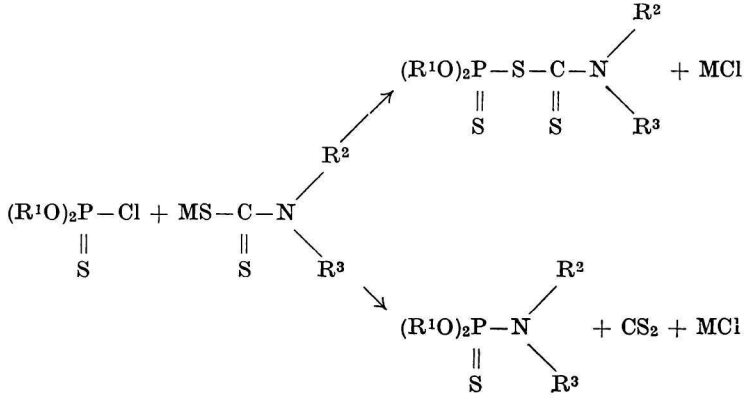
The synthesis of *S*-(*N*′,*N*′-dialkylthiocarbamoyl)(*N*,*N*-dialkylamido)ethyldithiophosphonates by reaction of (*N*,*N*-dialkylamido)ethylchlorothiophosphonate with alkali salt of *N*,*N*-dialkyldithiocarbamic acid is described. The synthesized compounds were tested for biological activity. *S*-(*N*′,*N*′-Dimethylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate was found to show high fungicidal activity towards *Phytophtora infestans*.

It is known from the literature [1] that the reaction of *O*,*O*-dialkyl chlorothiophosphates with alkali salt of *N*,*N*-dialkyldithiocarbamic acid gives *O*,*O*-dialkyl (*N*,*N*-dialkylamido)thiophosphate in larger amount beside *O*,*O*-dialkyl *S*-(*N*,*N*-dialkylthiocarbamoyl)dithiophosphate according to the Scheme 1.

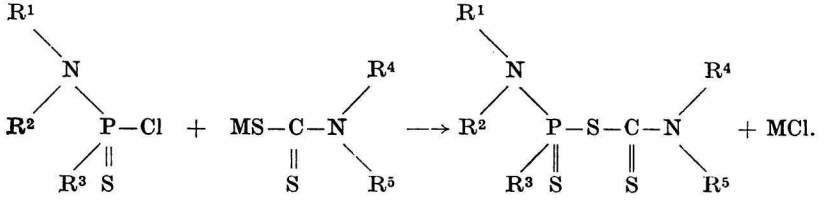


Scheme 1

Because of the mentioned side reaction, *O*,*O*-dialkyl *S*-(*N*,*N*-dialkylthiocarbamoyl)-dithiophosphates as pure compounds cannot be prepared. From similar compounds, *S*-(*N*′,*N*′-dialkylthiocarbamoyl) bis-(*N*,*N*-dialkylamido)dithiophosphates [2—4], *O*-alkyl *S*-(*N*,*N*-dialkylthiocarbamoyl)dithiophosphonates [5—7], *O*,*O*-dialkyl *S*-(*N*,*N*-dialkylthiocarbamoyl)dithiophosphates [8—11], and *S*-alkyl *S*-(*N*,*N*-dialkylthiocarbamoyl)-alkyltrithiophosphonates [12] are described in the literature as active insecticides and fungicides.

Searching for similar biological properties of other phosphonates led to the synthesis of *S*-(*N*′,*N*′-dialkylthiocarbamoyl) (*N*,*N*-dialkylamido)ethyldithiophosphonates by

treatment of (*N*,*N*-dialkylamido)ethylchlorothiophosphonate with alkali salt of *N*,*N*-dialkyldithiocarbamic acid in acetone according to the Scheme 2.



Scheme 2

It was found that this reaction gave exclusively the mentioned product. The synthesized compounds were practically not active as insecticides, acaricides, ovicides, and herbicides. The fungicidal activity of some compounds was interesting. Compound *V* was most active, even more active than the used standard Novozír (ED_{50} = 21 against ED_{50} = 39.8 with the standard) when tested on *Phytophtora infestans*. Sharvell test with compounds *I*, *V*, and *XII* gave orderly the same results as the standard Kaptan and so did the test with compound *I* on *Sclerotinia fructicola*. The antipowdery mildew efficacies with compounds *II*—*IV* and *XII* are worth mentioning.

Experimental

(*N*,*N*-Dialkylamido)ethylchlorothiophosphonate (0.05 mole) was added to alkali salt of *N*,*N*-dialkyldithiocarbamic acid (0.055 mole) in acetone (80 ml) under stirring. The reaction mixture was stirred under reflux for 2 hrs and after cooling poured into water (400 ml). The organic layer was extracted with benzene (100 ml). The benzene layer was washed with water. After drying it with sodium sulfate, benzene was distilled off under vacuum. The liquid residue was freed from benzene at 80°C and 0.1 torr during 20 min. When the residue was solid it was purified by crystallization.

The analytical and physicochemical data of the synthesized compounds are given in Table 1.

Biological activities of the synthesized compounds were tested on the following objects:

Insecticidal efficacy was followed on *Musca domestica* L., *Calandra granaria* L., systemic insecticidal efficacy on *Macrosyphoniella sanborni* THEOB., acaricidal efficacy on *Tetranychus urticae* KOCH, ovicidal efficacy on the eggs of *Tetranychus urticae* KOCH, and contact insecticidal efficacy on *Aphis fabae* SCOP.

Fungicidal efficacy was determined by *in vitro* as well as *in vivo* methods. The inherent efficacy was followed on the spores of *Sclerotinia fructicola* (WINT.) and on the spores of *Aspergillus niger* TIEGH, *Fusarium nivale* (FR.) CES., *Alternaria sp.*, and *Stemphylium sarcinoformae* (CAV) *Witshire* fungi by the Sharvell method. The antipowdery mildew efficacy was tested on the living plants of barley, sort Dunajský trh (*Erysiphe graminis* DC.), on cucumbers, sort Znojemské (*Erysiphe cichoracearum* DC.), and on tomatoes (*Phytophtora infestans de* BY).

The herbicidal efficacy was determined by the method of preemergence (into the soil) and postemergence (to the leaf) application on *Avena sativa*, *Polygonum persicaria*, *Fagopyrum sagitatum*, and *Sinapis alba*.

Methods for determination of biological activities on individual objects were published already [13, 14].

Table 1

Substituted ethyldithiophosphonates

No.	Compound	Formula	*M*	Calculated/ /found % P	Calculated/ /found % S	Yield [%]	M.p. [°C] (Kofler) (Solvent) n_D^{20}
I	*S*-(*N'*,*N'*-Dimethylthiocarbamoyl) (*N*,*N*-dimethylamido)ethyldithiophosphonate	$C_7H_{17}N_2PS_3$	256.36	12.08 11.94	37.45 37.69	78.0	70—72 (Cyclohexane)
II	*S*-(*N'*,*N'*-Diethylthiocarbamoyl) (*N*,*N*-dimethylamido)ethyldithiophosphonate	$C_9H_{21}N_2PS_3$	284.41	10.90 10.80	33.78 34.07	93.5	1.5774
III	*S*-(*N'*-Morpholinothiocarbamoyl) (*N*,*N*-dimethylamido)ethyldithiophosphonate	$C_9H_{19}N_2OPS_3$	298.40	10.33 10.56	32.00 31.62	88.4	1.5943
IV	*S*-(*N'*,*N'*-Dialylthiocarbamoyl) (*N*,*N*-diethylamido)ethyldithiophosphonate	$C_{13}H_{25}N_2PS_3$	336.49	9.22 9.61	28.52 28.90	64.3	1.5732
V	*S*-(*N'*,*N'*-Dimethylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate	$C_{10}H_{21}N_2PS_3$	296.42	10.44 10.34	32.41 32.80	96.3	92—93 (Cyclohexane)
VI	*S*-(*N'*,*N'*-Diethylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate	$C_{12}H_{25}N_2PS_3$	324.47	9.54 9.76	29.65 30.08	72.0	1.6120
VII	*S*-(*N'*-Methyl-*N'*-isopropylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphate	$C_{12}H_{25}N_2PS_3$	324.47	9.54 9.36	29.65 29.62	83.3	1.6098
VIII	*S*-(*N'*,*N'*-Diisopropylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphate	$C_{14}H_{29}N_2PS_3$	352.52	8.80 8.89	27.30 27.15	66.1	1.6002
IX	*S*-(*N'*,*N'*-Dialylthiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate	$C_{14}H_{25}N_2PS_3$	348.49	8.89 8.65	27.60 27.94	91.4	1.5987
X	*S*-(*N'*-Piperidinothiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate	$C_{13}H_{25}N_2PS_3$	336.49	9.22 8.94	28.52 29.08	97.2	82—84 (Ethanol)
XI	*S*-(*N'*-Morpholinothiocarbamoyl) (*N*-piperidino)ethyldithiophosphonate	$C_{12}H_{23}N_2OPS_3$	338.46	9.17 9.36	28.40 28.60	94.7	1.6123
XII	*S*-(*N'*,*N'*-Dimethylthiocarbamoyl) (*N*,*N*-dimethylamido)phenyldithiophosphonate	$C_{11}H_{17}N_2PS_3$	304.41	10.17 9.94	31.78 32.06	85.6	96—97 (Cyclohexane)

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