Preparation of S-[2,3-bis(phenylthio)maleimidomethyl]thio- and -dithiophosphates, their spectral and biological properties

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S-[2,3-bis(Phenylthio)maleimidomethyl]thio- and -dithiophosphates were prepared from N-bromomethyl-2,3-bis(phenylthio)maleimide and potassium salts of appropriate acids. Infrared and electronic spectra of the prepared compounds were evaluated. Linear relationship was found between $\nu(P=O)$ and $\Sigma\sigma^*$ of the substituents on phosphorus. Insecticidal, acaricidal, ovicidal, and fungicidal activities were determined.

Были приготовлены S-[2,3-бис(фенилтио)малеинимидометил]тио- и -дитиофосфаты из N-бромметил-2,3-бис(фенилтио)малеинимида и калиевых солей тио- и дитиофосфорной кислот. Проведена обработка инфракрасных и электронных спектров приготовленных соединений и обнаружена линейная зависимость между волновым числом $\nu(P=O)$ и $\Sigma\sigma^*$ заместителей на атоме фосфора. Были определены инсектицидное, акарицидное, овицидное и фунгицидное действия полученных соединений.

This work is a continuation of the study of synthesis and pesticidal activities of compounds structurally similar to the known insecticide Imidan (O,O-dimethyl-S-phthalimidomethyldithiophosphate) [1] as well as of the effect of substituents on the stretching vibration of $\nu(P=O)$ in the infrared spectra [2].

The starting compounds for the preparation of thiophosphates *IV—XIII* and dithiophosphates *XIV—XVIII* (Table 1) were N-bromomethyl-2,3-bis(phenylthio)maleimide (*III*) and the potassium salts of appropriate acids as presented in Scheme 1.

I—III

IV—XVIII
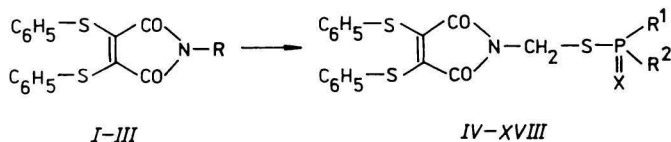
I R = H
II R = CH$_2$OH
III R = CH$_2$Br
For X, R^1, and R^2 see Table 1.

Scheme 1

Experimental

Infrared spectra of the prepared compounds in the region of 3000—500 cm^{-1} were measured on an IR-71 spectrophotometer (Zeiss, Jena) in tetrachloromethane. The absorption bands of the stretching $v(P=O)$ vibration in the region of 1300—1200 cm^{-1}, necessary for correlations, were measured on a UR-10 spectrophotometer (Zeiss, Jena) in tetrachloromethane and acetonitrile in such a way that the maximum of these absorption bands was ~75%. Measurements were performed in 0.18 mm cells and the apparatus was calibrated with polystyrene foil. The wavenumbers of the absorption bands $v(P=O)$ were read with the accuracy of ± 1 cm^{-1}. The electronic spectra of the compounds *II—XVIII* were measured in ethanol on a Specord UV VIS spectrophotometer (Zeiss, Jena) in the region of 200—700 nm; the concentration of compounds was 2×10^{-4}—3×10^{-5} mol l^{-1}.

Potassium salts of *O,O*-diphenyl phosphorothioic acid, *O*-ethyl-*O*-phenyl phosphorothioic acid, and *O*-methyl *N,N*-dimethylamidophosphorothioic acid were prepared from the chlorides of appropriate acids [3, 4] by hydrolysis with potassium hydroxide in aqueous dioxan [5]. The other potassium salts of *O,O*-dialkyl phosphorothioic acids were prepared from the appropriate *O,O*-dialkyl phosphites [6]. Potassium salts of *O,O*-dialkyl phosphorodithioic acids were prepared from the corresponding *O,O*-dialkyl phosphorodithioic acids [7].

N-Hydroxymethyl-2,3-bis(phenylthio)maleimide (II)

The mixture of 2,3-bis(phenylthio)maleimide (*I*) (31.3 g; 0.1 mol), 35% aqueous solution of formaldehyde (23.3 g; 0.2 mol), and pyridine (30 ml) was refluxed for 20 min under stirring. Water and pyridine were distilled off under reduced pressure. The orange oily residue was dissolved in chloroform and the solution was dried over anhydrous sodium sulfate. After removing the solvent by distillation, a viscous oil (32 g; 93 %) of $n_D^{20} = 1.6705$ was obtained. Crystallization from tetrachloromethane (the compound crystallized with difficulty) resulted in orange crystals of m.p. 104—107°C and R_f 0.32. For thin-layer chromatography on Silufol UV-254 (Lachema, Brno) the following solvent system was used: ethyl acetate—benzene—cyclohexane (7:20:10).

Table 1

Characteristics of the prepared organophosphorus compounds

Compound	X	R^1	R^2	Formula	M	Calculated/found		Yield %	n_D^{20}	R$_f$
						% P	% S			
IV	O	C$_6$H$_5$O	C$_6$H$_5$O	C$_{29}$H$_{22}$NO$_5$PS$_3$	591.66	5.23	16.26	92	a, b	0.57
						5.19	16.31			
V	O	C$_6$H$_5$O	C$_2$H$_5$O	C$_{25}$H$_{22}$NO$_5$PS$_3$	543.62	5.70	17.69	98	1.6360	0.39
						5.38	17.80			
VI	O	CH$_3$O	CH$_3$O	C$_{19}$H$_{18}$NO$_5$PS$_3$	467.52	6.62	20.58	91	1.6503	0.10
						6.60	20.61			
VII	O	C$_2$H$_5$O	C$_2$H$_5$O	C$_{21}$H$_{22}$NO$_5$PS$_3$	495.58	6.25	19.41	88	a, c	0.19
						6.40	19.53			
VIII	O	n-C$_3$H$_7$O	n-C$_3$H$_7$O	C$_{23}$H$_{26}$NO$_5$PS$_3$	523.62	5.92	18.37	88	1.6219	0.31
						5.62	18.97			
IX	O	n-C$_4$H$_9$O	n-C$_4$H$_9$O	C$_{25}$H$_{30}$NO$_5$PS$_3$	551.68	5.62	17.44	94	1.6031	0.39
						5.80	17.20			
X	O	iso-C$_4$H$_9$O	iso-C$_4$H$_9$O	C$_{25}$H$_{30}$NO$_5$PS$_3$	551.68	5.62	17.44	93	1.6005	0.41
						5.18	17.63			
XI	O	iso-C$_3$H$_7$O	iso-C$_3$H$_7$O	C$_{23}$H$_{26}$NO$_5$PS$_3$	523.63	5.92	18.37	98	1.6142	0.27
						6.19	19.01			

Table 1 (Continued)

Compound	X	R¹	R²	Formula	M	Calculated/found		Yield %	n_D^{20}	R_f
						% P	% S			
XII	O	*sec*-C_4H_9O	*sec*-C_4H_9O	$C_{25}H_{30}NO_5PS_3$	551.68	5.62	17.44	92	1.6052	0.37
						5.21	17.36			
XIII	O	CH_3O	$(CH_3)_2N$	$C_{10}H_{21}N_2O_4PS_3$	477.58	6.49	20.14	84	1.6332	0.07
						6.21	20.33			
XIV	S	CH_3O	CH_3O	$C_{19}H_{18}NO_4PS_4$	483.59	6.40	26.52	89	1.6651	0.70
						6.37	26.14			
XV	S	C_2H_5O	C_2H_5O	$C_{21}H_{22}NO_4PS_4$	511.65	6.05	25.07	98	1.6451	0.72
						5.96	25.16			
XVI	S	*n*-C_3H_7O	*n*-C_3H_7O	$C_{23}H_{26}NO_4PS_4$	539.69	5.74	23.76	93	1.6279	0.75
						5.94	23.43			
XVII	S	iso-C_3H_7O	iso-C_3H_7O	$C_{23}H_{26}NO_4PS_4$	539.69	5.74	23.76	90	1.6342	0.75
						5.53	23.42			
XVIII	S	iso-C_4H_9O	iso-C_4H_9O	$C_{25}H_{30}NO_4PS_4$	576.76	5.46	22.59	94	1.6232	0.79
						5.26	22.34			

a) Crystallization from methanol; *b*) m.p. 91—93°C; *c*) m.p. 75—78°C.

For $C_{17}H_{13}NO_3S_2$ (343.43) calculated: 59.46% C, 3.82% H, 4.08% N; found: 58.96% C, 4.05% H, 4.47% N; $v_s(CO)$ 1775, $v_{as}(CO)$ 1721, $v(OH)$ 3600.

N-Bromomethyl-2,3-bis(phenylthio)maleimide (III)

To the solution of *II* (34.3 g; 0.1 mol) in dry benzene (50 ml), phosphorus tribromide (13.5 g; 0.05 mol) was added within 20 min under stirring in such a way that the temperature of the reaction mixture did not rise above 30°C. Then the reaction mixture was boiled for 2 h excluding the atmospheric moisture. The benzene layer was decanted from phosphorus acid and evaporated. The formed crystals were filtered, washed with the solution of benzene—hexane (1:4) and dried. Evaporation of the supernatant gave another portion of *III*. Crystallization from toluene resulted in orange crystals (20.3 g; 50%) of m.p. 128—129°C and R_f 0.71 using the same solvent system for thin-layer chromatography as with the compound *II*.

For $C_{17}H_{22}NO_2S_2Br$ (406.33) calculated: 50.13% C, 2.97% H, 3.44% N; found: 49.91% C, 2.98% H, 3.80% N; $v_s(CO)$ 1781, $v_{as}(CO)$ 1730, $\lambda(\varepsilon)$ 208 (33 500), 250 (17 500), 420 (6550).

S-[2,3-bis(Phenylthio)maleimidomethyl]thio- (IV—XIII) and -dithiophosphates (XIV—XVIII)

The mixture of potassium salts of the corresponding acids (0.012 mol) and *III* (4.1 g; 0.01 mol) was stirred in 2-butanone (15 ml) for 20 min at room temperature (20—25°C). The formed potassium bromide was filtered, washed with a small amount of 2-butanone and the supernatant was shaked with water (120 ml) in a separating funnel. The product was extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate and filtered. The solvent was distilled off under reduced pressure and the product (a yellow viscous oil) was dried at 80°C and 26 Pa. The purity of products was checked by thin-layer chromatography on Silufol UV-254 (Lachema, Brno) using ethyl acetate—benzene—cyclohexane (7:20:10) as solvent system. The characteristics of the prepared thio- and dithiophosphates are presented in Table 1, infrared and electronic spectral data are given in Table 2.

Pesticidal activity

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 *Aphis fabae* SCOP 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. Insecticidal, acaricidal, and ovicidal activities were determined after [8, 9]. Fungicidal activity was determined by the *in vitro* and *in vivo* methods. Inherent activity was followed on spores of *Sclerotinia fructicola* (WINT.) by the method after Sharvell using Kaptan (3a,4,7,7a-tetrahydro-*N*-trichloromethanesulfenylphthalimide) as standard. The antipowdery mildew activity was followed by spraying the living plants of spring barley, sort Dunajský trh (*Erysiphe graminis* DC.) using Chloraniformethane (1-(3,4-dichloroanilino)-1-formylamino-2,2,2-trichloroethane) as standard, by spraying cucumbers *(Erysiphe polyphaga Hammarlund)* using Dinokap (2,4-dinitro-6-octylphenyl crotonate + 2,6-dinitro-4-octylphenyl crotonate) as standard, and by spraying tomatoes (*Phytophthora infestans* De BY) using Mankozeb (Mn(II) and Zn(II) ethylenebisdithiocarbamates in the ratio of 7:1) as standard [10]. The activity on *Tilletia foetida, Botrytis cinerea,* and *Fusarium nivale* was determined after [11] by the zone method using Kaptan as standard. The systemic activity on *E. polyphaga* and *P. infestans* was determined by watering after [11] using Tridemorf (*N*-tridecyl-2,6-dimethylmorpholine) as standard.

Table 2

Infrared ($\bar{v}$, cm^{-1}) and electronic spectral data of the organophosphorus compounds

Compound	v_s(CO)	μ_{as}(CO)	v(P=S)	v(PO—C)	λ_{max}, nm (ε_{max}, l mol^{-1} cm^{-1})		
IV	1777	1727	—	1164 1205	208 (35 000)	251 (14 000)	424 (4500)
V	1778	1726		1166 1200 1026	208 (30 000)	250 (13 750)	422 (4100)
VI	1780	1729	—	1027	209 (26 000)	250 (15 000)	420 (4500)
VII	1780	1728	—	1021	209 (23 100)	249 (13 500)	420 (4250)
VIII	1780	1729	—	1000	209 (22 500)	249 (13 750)	420 (4250)
IX	1779	1726	—	1025	209 (23 800)	249 (14 600)	420 (4500)
X	1778	1726	—	1001	208 (27 500)	249 (15 000)	420 (4600)
XI	1780	1727	—	986	209 (20 900)	249 (15 000)	420 (4250)
XII	1777	1726	—	985	208 (23 800)	249 (14 700)	420 (4400)
XIII	1777	1724	—	1027	208 (22 200)	250 (11 700)	420 (3750)
XIV	1780	1728	653	1026	209 (31 500)	249 (14 750)	424 (4500)
XV	1778	1726	652	1014	209 (27 500)	249 (14 800)	422 (4500)
XVI	1778	1726	655	987	208 (31 300)	248 (15 900)	424 (4650)
XVII	1777	1726	648	973	209 (32 500)	249 (15 200)	422 (4500)
XVIII	1778	1725	668	996	210 (29 500)	249 (15 700)	425 (4900)

Results and discussion

The initial *N*-bromomethyl-2,3-bis(phenylthio)maleimide (*III*) was prepared from 2,3-bis(phenylthio)maleimide (*I*) [12]. Hydroxymethylation of *I* with formal-

dehyde after [13] was not successful. High yields in this reaction were obtained in the presence of pyridine, which, as a part of the solvent (water—pyridine), served also as a catalyst. Hydroxymethylation of imides with formaldehyde in the presence of triethylamine as catalyst has been already described [14]. We prepared the compound *III* from *II* by treatment with phosphorus tribromide in benzene after the procedure described in [15]. The components of the reaction mixture determined by thin-layer chromatography on Silufol UV-254 (Lachema, Brno) in the system ethyl acetate—benzene—cyclohexane (7 : 10 : 20) indicated that the reaction of *III* with potassium thio- and dithiophosphates proceeded with high yields already at room temperature within 20—25 min. From the data in [16, 17] it is evident that the authors carried out analogous reactions at higher temperatures (60—80°C) and longer reaction time (several hours).

The substituents R^1 and R^2 did not influence the positions of bands in the electronic spectra of the compounds *II—XVIII*. In the i.r. spectra of the organophosphorus compounds *V—XVIII* (Table 2), an intensive absorption band belonging to the stretching vibration of $v(PO—Alkyl)$ was observed in the region of 1030—970 cm^{-1} [18, 19]. The absorption bands of medium intensity in the region of 1205—1164 cm^{-1} with the compounds *IV* and *V* were attributed to the stretching vibration of $v(PO—Aryl)$ [18, 19]. The intensive band at 944 cm^{-1} with the compound *IV* and the band of medium intensity at 934 cm^{-1} with the compound *V* belonged to the stretching vibration of $v(P—O \ Aryl)$ [19]. In the region of the stretching $C=O$ vibration two absorption bands were observed. The more intensive band at lower wavenumbers belonged to the asymmetric and the less intensive one at higher wavenumbers to the symmetric vibration of the

Table 3

Wavenumbers $v(P=O)$ of thiophosphates

Compound	$v_1(P=O)^a$	$v_2(P=O)^a$	$v(P=O)^b$	$v_2(P=O) - v_1(P=O)$	$v(P=O)^c$	$\sigma^*(R^1) + \sigma^*(R^2)$
IV	1264	1289	1276.5	25	1278	4.48
V	1256	1275	1265.5	19	1264	3.88
VI	1253	1270	1261.5	17	1259	3.46
VII	1249	1263	1256.0	14	1254	3.28
VIII	1249	1264	1256.5	15	1250	3.14
IX	1247	1261	1254.0	14	1254	3.10
X	1248	1260	1254.0	12	1253	3.04
XI	1246	1260	1253.0	14	1251	3.02
XII	1247	1259	1253.0	12	1251	2.98
XIII	1238	—	1238.0	—	1233	2.35

a) Measured in tetrachloromethane; *b*) arithmetic mean of the wavenumbers $v_1(P=O)$ and $v_2(P=O)$; *c*) measured in acetonitrile.

dicarbonyl system [20]. For dithiophosphates the absorption band of the medium intensity belonging to the stretching $P = S$ vibration [18] and for thiophosphates the absorption band of medium intensity belonging to the stretching $P = O$ vibration [21] were characteristic. The absorption band $v(P = O)$ was observed in the i.r. spectra measured in tetrachloromethane (nonpolar solvent) as well as in acetonitrile (polar solvent) (Table 3). It was found that $v(P = O)$ in the spectra measured in tetrachloromethane was a doublet and that the distance between the maxima of these bands (in cm^{-1}) linearly decreased with the decreasing sum of the Taft σ^* constants of the substituents R^1 and R^2. With the compound XIII, where $\sigma^*(R^1) + \sigma^*(R^2) = 2.35$ (the lowest value of $\Sigma\sigma^*$), the doublet of bands $v(P = O)$ was not distinguishable. The absorption band of $v(P = P)$ in the spectra measured in acetonitrile was observed at the wavenumber approximately corresponding to the arithmetic mean of the wavenumbers v_1 and v_2 obtained in tetrachloromethane (Table 3). The wavenumber $v(P = O)$ can be correlated with the sum of the Taft σ^* constants of the substituents bound on phosphorus [22]. The wavenumbers $v(P = O)$ were correlated only with the Taft σ^* constants of the substituents R^1 and R^2 because the Taft σ^* constant of the third substituent, bound via sulfur to phosphorus, is not known. The Taft σ^* constants of the substituents R^1 and R^2 were taken from the works [2, 23—25]. For the correlation of $v(P = O)$, measured in tetrachloromethane, with $\Sigma\sigma^*$ the arithmetic means of the wavenumbers v_1 and v_2 were used; the value of the slope ϱ was in a good agreement with the slope of the relationship given by Griffin [22] $v(P = O) = 16.80 \ \Sigma\sigma^* + 1198$ because in both cases the wavenumbers $v(P = O)$ were measured in nonpolar solvent. The statistical parameters of the linear correlation between $v(P = O)$ and $\Sigma\sigma^*$ in tetrachloromethane and acetonitrile are presented in Table 4.

The contact insecticidal activity on M. domestica, C. granaria, and A. fabae with the prepared compounds at $100 \rightarrow 5000$ p.p.m. was low and therefore not comparable with the used standard. Similar results were obtained in systemic insecticidal activity on A. fabae. The highest activity (acaricidal and ovicidal) was

Table 4

Statistical parameters of the linear correlation between $v(P = O)$ and $\Sigma\sigma^*$ with thiophosphates IV—XIII

Solvent	r	ϱ	s_ϱ	q	s_q	s
Tetrachloromethane	0.961	16.60	1.69	1202.5	17.5	2.91
Acetonitrile	0.980	19.49	1.40	1180.9	16.2	2.41

r — correlation coefficient; ϱ — slope; s_ϱ — standard deviation ϱ; q — intercept on the axis of wavenumbers; s_q — standard deviation q; s — residual scattering.

Table 5

Acaricidal and ovicidal activities (LD_{50} in p.p.m.) of some organophosphorus compounds

Compound	*Tetranychus urticae* KOCH	
	Females	Eggs
IV	>1000	100
V	850	1000
VI	60	1200
VII	70	1000
VIII	950	1000
IX	>1000	1000
X	850	1000
XI	1000	3600
XII	450	1000
XV	380	4200
XVIII	>1000	1000
Karbofenthion	0.98	22

observed with the compounds *VI* and *VII* on *T. urticae* (Table 5). In tests for fungicidal activity measurable values were obtained only with *VI*; on *B. cinerea* it was ~75% activity of the standard (Kaptan).

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