

Synthesis and biological activity of *O,O*-dialkyl *S*-(5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio- and dithiophosphates

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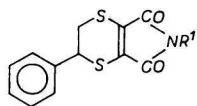
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*Dedicated to Professor J. Majer, Corresponding Member of the
Slovak Academy of Sciences, on his 50th birthday*

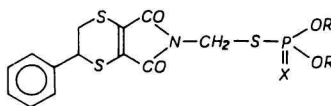
O,O-Dialkyl *S*-(5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio-phosphates and *O,O*-dialkyl *S*-(5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) dithiophosphates were prepared from *N*-chloromethyl-5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide and potassium salts of *O,O*-dialkyl thiophosphoric and *O,O*-dialkyl dithiophosphoric acids. Electronic and infrared spectra of all the prepared compounds and in the case of compounds *III*, *IV*, and *IX* also ¹H-NMR spectra were interpreted.

Были синтезированы *O,O*-диалкил-*S*-(5-фенил-5,6-дигидро-1,4-дйтиин-2,3-дикарбоксимидометил)тио- и дитиофосфаты, исходя из *N*-хлорметил-5-фенил-5,6-дигидро-1,4-дйтиин-2,3-дикарбоксимида и калиевой соли *O,O*-диалкилтио- и дитиофосфорной кислот. Исследованы электронные, инфракрасные, а, в случае соединений *III*, *IV* и *IX*, также ¹H-ЯМР спектры.

In [1, 2] we described the synthesis of *O,O*-dialkyl *S*-(5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio- and dithiophosphates and *O,O*-dialkyl *S*-(5-methyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio- and di-



I—III



IV—XIII

I. R¹ = H, II. R¹ = CH₂OH, III. R¹ = CH₂Cl.
R, X (see Table 1).

Scheme 1

thiophosphates which were structurally similar to the known insecticide "Imidan" (*O,O*-dimethyl-*S*-phthalimidomethyl dithiophosphate). The pesticidal activity of these compounds was found to be lower than that of the standard Imidan.

The present work deals with the synthesis of *O,O*-dialkyl *S*-(5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio- and dithiophosphates *IV—XIII* (Scheme 1) and with examination of their pesticidal activity.

Experimental

Infrared spectra were measured on a Zeiss UR-10 spectrophotometer in tetrachloroethylene. The concentration of the measured compounds was chosen so that the absorption maximum of the most intensive band in the region 1900—1600 cm^{-1} was 75%. 0.18 mm cells were used and the apparatus was calibrated with a polystyrene foil. Wavenumbers were read with $\pm 0.5 \text{ cm}^{-1}$ accuracy.

Electronic spectra of *II* and *III* were measured in dry methanol and those of the organophosphorus compounds *IV—XIII* in dry ethanol on a Specord UV VIS Zeiss spectrophotometer in the region 200—750 nm; the concentration of compounds was 4×10^{-5} M.

$^1\text{H-NMR}$ spectra were taken on a Tesla BS-487A spectrophotometer at 80 MHz in deuterated chloroform. The chemical shift was read with an accuracy of ± 0.02 p.p.m. and hexamethyldisiloxane was used as standard.

The starting 5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide (*I*) was prepared according to [3] and the potassium salts of *O,O*-dialkyl thiophosphoric and *O,O*-dialkyl dithiophosphoric acids were prepared according to [4, 7].

N-Hydroxymethyl-5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide (*II*)

The mixture of 5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide (*I*) (13.17 g; 0.05 mole), 10% aqueous solution of formaldehyde (30 g; 0.1 mole), and a few drops of triethylamine was refluxed for 2 hrs under stirring. Then the reaction mixture was cooled and the yellow solid product was filtered off, washed with water, and dried. Yield after crystallization from methanol 13.8 g (94%), m.p. 140—146°C. The product was purified chromatographically on a column of silica gel L 40/100 (Lachema, Brno) using ethyl acetate—carbon tetrachloride (1:1) as eluent. Melting point after purification 144—148°C.

For $\text{C}_{13}\text{H}_{11}\text{NO}_3\text{S}_2$ (293.37) calculated: 53.23% C, 3.78% H, 4.77% N, 21.86% S; found: 52.70% C, 3.91% H, 5.01% N, 21.91% S; $\nu(\text{CO})$ 1775, 1723, $\nu(\text{C}=\text{C})$ 1558, $\nu(\text{OH})$ 3600; $\lambda(\epsilon)$ 214 (11500), 249 (8620), 410 (2500).

N-Chloromethyl-5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide (*III*)

Freshly distilled thionyl chloride (59.48 g; 0.5 mole) and *II* (14.67 g; 0.05 mole) were refluxed for 2 hrs under stirring. Then the reaction mixture was poured onto crushed ice (300 g) and stirred for 20—30 min. The formed crude oil was separated, dissolved in dichloromethane, and extracted with water. The organic layer was dried with anhydrous sodium sulfate and filtered. The solvent was distilled off under reduced pressure and the product (oil) solidified within 30 min. Crystallization from carbon tetrachloride gave yellow crystals with m.p. 139—142°C. The product was purified also on a

column of silica gel L 40/100 (Lachema, Brno) using chloroform as eluent. The m.p. after purification was 144–145°C.

For $C_{13}H_{10}NO_2S_2Cl$ (311.81) calculated: 50.08% C, 3.23% H, 4.49% N, 20.57% S, 11.37% Cl; found: 50.37% C, 3.31% H, 4.22% N, 20.68% S, 11.12% Cl; $\nu(CO)$ 1775, 1723, $\nu(C=C)$ 1553; $\lambda(\epsilon)$ 214 (15010), 256 (8670), 147 (2880); ^1H-NMR . δ (p.p.m.) (CH_2-S) 5.28, ($CH-S$) 4.40, (CH_{ar}) 7.28.

O,O-Dialkyl S-(5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximidomethyl) thio- (IV—VIII) and dithiophosphates (IX—XIII)

Potassium salts of *O,O*-dialkyl thiophosphoric or dithiophosphoric acid (0.017 mole) and *III* (4.37 g; 0.014 mole) were heated at 60°C in ethyl methyl ketone (20 ml) for 6 hrs under stirring. (In the case of *IX* the reaction temperature was 20°C.) The reaction mixture was cooled to 20°C and poured into water (150 ml) under stirring. The precipitated oil was extracted with chloroform. The organic layer was separated, dried with anhydrous sodium sulfate and filtered. Then the solvent was distilled off under reduced pressure and the obtained yellow viscous oil was dried at 80°C and 26.7 Pa. The products were purified on a column of silica gel L 40/100 (Lachema, Brno) using ethyl acetate—carbon tetrachloride (1:1) as eluent for thiophosphates (*IV—VIII*) and chloroform for dithiophosphates.

^1H-NMR δ (p.p.m.) *IV*: (CH_3O) 3.70, (CH_2-S) 3.30, ($CH-S$) 4.38, ($N-CH_2-S$) 4.80, (CH_{ar}) 7.26.

Characterization of the prepared thiophosphates and dithiophosphates and their i.r. and electronic spectra are presented in Tables 1 and 2.

Insecticidal, acaricidal, ovicidal, and fungicidal activities of the synthesized compounds were followed according to the methods published in [10].

Results and discussion

N-Chloromethyl-5-phenyl-5,6-dihydro-1,4-dithiin-2,3-dicarboximide (*III*) and the corresponding potassium salts of *O,O*-dialkyl thiophosphoric and *O,O*-dialkyl dithiophosphoric acids [4–7] were the starting substances for preparation of thiophosphates (*IV—VIII*) and dithiophosphates (*IX—XIII*) (Table 1). The *N*-chloromethyl derivative (*III*) reacted with these salts almost quantitatively.

In the i.r. spectra of the prepared organophosphorus compounds (Table 2) a band belonging to the stretching vibration of the double bond of 5,6-dihydro-1,4-dithiine ring was observed at 1556–1558 cm^{-1} (the same position with all compounds). In the region of the $C=O$ stretching vibration two absorption bands appeared: the more intensive band at 1721–1719 cm^{-1} belonged to the asymmetrical and the less intensive one at 1771–1775 cm^{-1} to the symmetrical vibrations of the dicarbonyl system [8]. An absorption band of medium intensity belonging to the stretching vibration of $P-O-C$ [9] was observed with thiophosphates (*IV—VIII*) as well as dithiophosphates (*IX—XI*). It can be seen from the data in Table 2 that the $P-O-C$ band position depended on the nature of the alkyl and alkoxy groups.

Table 1

Characterization of the prepared organophosphorus compounds

No.	R	X	Formula	M	Calculated/found		Yield %	M.p. °C/solvent n_D^{20}	R_F
					% P	% S			
IV	CH ₃	O	C ₁₅ H ₁₆ NO ₅ PS ₃	417.46	7.42	23.04	95	86—89	0.32
V	C ₂ H ₅	O	C ₁₇ H ₂₀ NO ₅ PS ₃	445.52	7.65	22.83	91	Methanol	0.42
					7.20	21.90		133—135	
VI	<i>n</i> -C ₃ H ₇	O	C ₁₉ H ₂₄ NO ₅ PS ₃	473.57	6.54	20.31	90	Methanol	0.57
					6.82	20.40		61—63	
VII	iso-C ₃ H ₇	O	C ₁₉ H ₂₄ NO ₅ PS ₃	473.57	6.54	20.31	82	Diethyl ether	0.51
					6.77	19.95		78—81	
VIII	iso-C ₄ H ₉	O	C ₂₁ H ₂₈ NO ₅ PS ₃	501.63	6.18	19.18	79	Diethyl ether	0.69
					6.10	19.33		1.5911	
IX	CH ₃	S	C ₁₅ H ₁₆ NO ₄ PS ₄	433.53	7.14	29.58	92	1.6578*	0.83
					6.81	29.93			
X	C ₂ H ₅	S	C ₁₇ H ₂₀ NO ₄ PS ₄	461.58	6.71	27.79	85	115—118	0.87
					6.52	27.80		Carbon tetrachloride	
XI	<i>n</i> -C ₃ H ₇	S	C ₁₉ H ₂₄ NO ₄ PS ₄	489.64	6.33	26.19	84	82—84	0.90
					6.10	25.93		Carbon tetrachloride	
XII	iso-C ₃ H ₇	S	C ₁₉ H ₂₄ NO ₄ PS ₄	489.64	6.33	26.19	85	111—113	0.89
					6.50	25.98		Carbon tetrachloride	
XIII	iso-C ₄ H ₉	S	C ₂₁ H ₂₈ NO ₄ PS ₄	517.69	5.98	24.78	83	1.6110	0.91
					6.17	24.52			

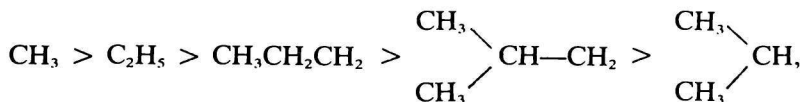
* n_D^{35} .

Table 2

Infrared and electronic spectra of the synthesized organophosphorus compounds

No.	$\bar{\nu}$, cm^{-1}					λ_{max} (ϵ) nm		
	$\nu_s(\text{CO})$	$\nu_{\text{as}}(\text{CO})$	$\nu(\text{C}=\text{C})$	$\nu(\text{P}=\text{X})$	$\nu(\text{P}-\text{O}-\text{C})$			
IV	1776	1720	1556	1262	1028	214 (20200)	262 (10520)	422 (3250)
V	1775	1720	1557	1260	1019	213 (21200)	264 (10610)	422 (2870)
VI	1776	1721	1558	1257	988	212 (21600)	263 (10500)	420 (3020)
VII	1775	1720	1558	1255	986	212 (18900)	264 (9500)	420 (2750)
VIII	1775	1719	1557	1256	1006	214 (24200)	262 (12850)	420 (3250)
IX	1776	1720	1557	653	1023	214 (20600)	265 (8030)	422 (2320)
X	1776	1719	1558	654	1016	214 (23600)	265 (9900)	422 (2660)
XI	1775	1720	1557	661	987	214 (24000)	265 (10050)	422 (2750)
XII	1775	1720	1558	649	973	214 (22800)	264 (9500)	422 (2340)
XIII	1775	1720	1557	666	998	214 (25600)	264 (10500)	422 (3100)

The absorption band in the region $1262\text{--}1255\text{ cm}^{-1}$ was attributed to the stretching vibration of $\text{P}=\text{O}$ and the wavenumber values of this vibration decreased in the following order



i.e. in the same order as the Taft's constants σ^* of these substituents. With dithiophosphates a band of medium intensity belonging to $\text{P}=\text{S}$ stretching vibration was observed at $666\text{--}649\text{ cm}^{-1}$

The solutions of the prepared organophosphorus compounds in benzene, chloroform, and other solvents were intensively fluorescent.

The position of the band in the visible region of the electronic spectra was not influenced by the alkyl groups. In the u.v. region two bands were observed: the ϵ values of the first band were higher than those of the second one.

Tests for insecticidal, acaricidal, ovicidal, and fungicidal activities showed that the introduction of a phenyl group into the position 5 of the 5,6-dihydro-1,4-dithiine ring resulted in an essential decrease of activity. Only the acaricidal activity of the compound *V* on *Tetranychus urticae* KOCH was comparable to the activity of the standard PCPBS (*p*-chlorophenyl benzenesulfonate).

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