

SYNTHESIS, SPECTRAL PROPERTIES AND PESTICIDE EFFECT
OF PYRIDAZINYL-4-OXY-1,3,2-DIOXAPHOSPHOLANE-2-THIONE
AND 1,3,2-DIOXAPHOSPHORINANE-2-THIONES

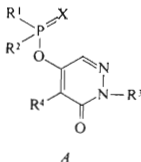
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The synthesis of new 2-(1-alkyl, phenyl-5-alkoxy, alkylthio, chloro-6-oxo-1*H*-pyridazinyl-4-oxy)-1,3,2-dioxaphospholane-2-thiones and 1,3,2-dioxaphosphorinane-2-thiones is described. The synthesized products were characterized by IR and UV spectral data and their contact and systemic insecticide, acaricide, ovicide and fungicide activities were measured, the highest being found the ovicide effect.

The hitherto investigated relation between the structure and pesticide activity of pyridazin-4-yl esters of organophosphorous acids of general formula *A* showed that the pesticide effect is influenced in a considerable degree by all substituents $R^1 - R^4$



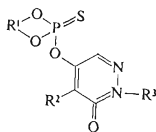
and X. The highest contact insecticide, acaricide and ovicide effects were found with compounds having $R^1 =$ ethyl, alkoxy, $R^2 =$ alkoxy, N-alkylamido, $R^3 =$ = alkyl, phenyl, benzyl, $R^4 =$ alkoxy, X = oxygen, sulfur. The highest fungicide activity displayed compounds with $R^1 =$ alkyl, alkoxy, N,N-dimethylamido, $R^2 =$ = alkoxy, N,N-dimethylamido, $R^3 =$ methyl, $R^4 =$ methoxy, ethylthio, X = oxygen, sulfur¹⁻⁴.

In continuation of our project dealing with the synthesis and pesticide activity of pyridazin-4-yl organophosphorates our endeavour was focussed on the synthesis of substances of general formula *B* having phosphorus incorporated in the heterocyclic ring.

We investigated the consequence of a structural change on pesticide activity and measured the IR and UV spectra of the prepared compounds. The racemate of 2,3-

butanediol ($[\alpha]_D^{25} + 0.2$) was used for preparation of 4,5-dimethyl-2-chloro-1,3,2-dioxaphospholane-2-thione; in an analogous way prepared 4,5-dimethyl-2-chloro-1,3,2-dioxaphospholane-2-thione and *III-V* were racemates, as well.

The desired products were synthesized from 2-chloro-1,3,2-dioxaphospholane-2-thione or 2-chloro-1,3,2-dioxaphosphorinane-2-thione and sodium or potassium 1-alkyl, phenyl-5-alkoxy, alkylthio, chloro-6-oxo-1*H*-pyridazin-4-ol in acetonitrile. The most part of the prepared compounds were crystalline products; liquids were purified by column chromatography according to⁵ (Table I). The IR spectral data were interpreted according to⁶. All spectra were measured in chloroform, some of them also in tetrachloromethane; the latter made it impossible to read vibrations $\nu_{as}(\text{OPO})$ and $\nu(\text{P}=\text{S})$ due to an overlapping absorption of the solvent. Reading of $\nu(\text{P}=\text{S})$



B

Formula B

	R ¹	R ²	R ³
<i>I</i>	CH ₂ -CH ₂	CH ₃ O	CH ₃
<i>II</i>	CH ₂ -CH ₂	CH ₃ O	C ₆ H ₅
<i>III</i>	CH(CH ₃)-CH(CH ₃)	CH ₃ O	CH ₃
<i>IV</i>	CH(CH ₃)-CH(CH ₃)	CH ₃ O	C ₆ H ₅
<i>V</i>	CH(CH ₃)-CH(CH ₃)	Cl	C ₆ H ₅
<i>VI</i>	CH ₂ -CH ₂ -CH(CH ₃)	CH ₃ O	CH ₃
<i>VII</i>	CH ₂ -CH ₂ -CH(CH ₃)	Cl	CH ₃
<i>VIII</i>	CH ₂ -CH ₂ -CH(CH ₃)	CH ₃ O	C ₆ H ₅
<i>IX</i>	CH ₂ -CH ₂ -CH(CH ₃)	Cl	C ₆ H ₅
<i>X</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	H	CH ₃
<i>XI</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	CH ₃ O	CH ₃
<i>XII</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	Cl	CH ₃
<i>XIII</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	C ₂ H ₅ O	CH ₃
<i>XIV</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	C ₂ H ₅ S	CH ₃
<i>XV</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	C ₃ H ₇ S	CH ₃
<i>XVI</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	Cl	C ₂ H ₅
<i>XVII</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	CH ₃ O	C ₆ H ₁₁
<i>XVIII</i>	CH ₂ -C(CH ₃) ₂ -CH ₂	CH ₃ O	C ₆ H ₅

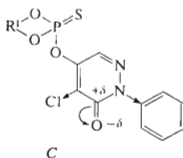
TABLE I

2-1-Alkyl, Phenyl-5-alkoxy, Alkylthio, Chloro-6-oxo-1*H*-pyridazinyl-4-oxy-1,3,2-dioxaphospholane, (phosphorinane)-2-thiones

Compound	Formula (mol. weight)	Calculated/Found			M.p., °C (yield, %)
		% P	% S	% N	
<i>I</i>	C ₈ H ₁₁ N ₂ O ₅ PS (278.2)	11.13	11.52	10.07	66–67
		11.28	11.81	10.06	(81.2)
<i>II</i>	C ₁₃ H ₁₃ N ₂ O ₅ PS (340.3)	9.10	9.42	8.23	168–170
		9.20	9.81	8.10	(59.1)
<i>III</i>	C ₁₀ H ₁₅ N ₂ O ₅ PS (306.2)	10.11	10.47	9.14	1.5421 ^a
		10.23	10.69	9.44	(68.3)
<i>IV</i>	C ₁₅ H ₁₇ N ₂ O ₅ PS (368.3)	8.41	8.70	7.61	91–92
		8.60	8.71	8.01	(71.2)
<i>V</i>	C ₁₄ H ₁₄ ClN ₂ O ₄ PS (372.7)	8.31	8.60	7.52	110–111
		8.41	8.80	7.68	(69.1)
<i>VI</i>	C ₁₀ H ₁₅ N ₂ O ₅ PS (306.3)	10.11	10.47	9.14	1.5541 ^a
		9.90	10.32	9.02	(89.6)
<i>VII</i>	C ₉ H ₁₂ ClN ₂ O ₄ PS (310.7)	9.97	10.32	9.02	78–80
		10.06	10.21	9.20	(84.7)
<i>VIII</i>	C ₁₅ H ₁₇ N ₂ O ₅ PS (368.3)	8.41	8.70	7.61	74–76
		8.43	8.71	7.60	(88.0)
<i>IX</i>	C ₁₄ H ₁₄ ClN ₂ O ₄ PS (372.7)	8.31	8.60	7.52	136–138
		8.65	8.81	7.68	(60.2)
<i>X</i>	C ₁₀ H ₁₅ N ₂ O ₄ PS (290.5)	10.67	11.04	9.65	114–115
		10.55	11.33	9.51	(84.6)
<i>XI</i>	C ₁₁ H ₁₇ N ₂ O ₅ PS (320.3)	9.67	10.01	8.74	98–99
		9.65	10.19	8.93	(72.6)
<i>XII</i>	C ₁₀ H ₁₄ ClN ₂ O ₄ PS (324.7)	9.54	9.87	8.63	162–163
		9.52	10.02	8.86	(83.0)
<i>XIII</i>	C ₁₂ H ₁₉ N ₂ O ₅ PS (337.5)	9.26	9.58	8.38	95–96
		9.16	9.65	8.64	(84.2)
<i>XIV</i>	C ₁₂ H ₁₉ N ₂ O ₄ PS ₂ (350.4)	8.84	18.30	7.99	109–110
		8.76	18.53	7.93	(76.8)
<i>XV</i>	C ₁₃ H ₂₁ N ₂ O ₄ PS ₂ (364.4)	8.50	18.09	7.90	116–117
		8.55	17.76	8.06	(90.1)
<i>XVI</i>	C ₁₁ H ₁₆ ClN ₂ O ₄ PS (338.7)	9.14	9.47	8.27	130–131
		8.98	9.61	8.47	(86.3)
<i>XVII</i>	C ₁₆ H ₂₅ N ₂ O ₅ PS (388.4)	7.97	8.25	7.21	110–112
		7.88	8.34	7.31	(69.8)
<i>XVIII</i>	C ₁₆ H ₁₉ N ₂ O ₅ PS (382.3)	8.10	8.39	7.33	150–151
		8.24	8.59	7.42	(90.2)

^a n_D²⁰.

stretching vibration at about 700 cm^{-1} was, for the same reason, impossible also in chloroform. Characteristic of all substances is the stretching vibration between $1636-1670$ and $1645-1684\text{ cm}^{-1}$ in chloroform and tetrachloromethane, respectively. Position of the $\nu(\text{C}=\text{O})$ stretching vibration is mainly influenced by the substituent R^2 , what has already been ascertained; in addition correlativeness with Taft constants⁴ was found. The substituent R^3 less influenced this position. As being found, substituent R^1 also influenced the $\nu(\text{C}=\text{O})$ stretching vibration, what is quite surprising; compounds *V* and *IX* ($\text{R}^2 = \text{Cl}$, $\text{R}^3 = \text{C}_6\text{H}_5$) form exceptions; here the wave number does not change either in CHCl_3 or in CCl_4 . This fact can be explained by the presence of strong electron-accepting Cl and C_6H_5 groups bound to carbon or nitrogen in the neighbourhood of carbonyl group; these considerably took part in lowering the electron density at carbon of the carbonyl group, so that the effect of substituent R^1 was negligible. On the other hand, the effect of substituent was not



manifested, if phenyl group was replaced by methyl group. The difference with compounds *VII* and *XII* ($\text{R}^2 = \text{Cl}$, $\text{R}^3 = \text{CH}_3$) made already 8 cm^{-1} . Like differences were observed with compounds *I*, *III*, *VI*, and *XI* ($\text{R}^2 = \text{CH}_3\text{O}$, $\text{R}^3 = \text{CH}_3$) and *II*, *IV*, *VIII*, and *XVIII* ($\text{R}^2 = \text{CH}_3\text{O}$, $\text{R}^3 = \text{C}_6\text{H}_5$). The effect of substituent R^1 on the wave number of $\nu(\text{C}=\text{O})$ stretching vibration was due to a spatial arrangement of the molecule. All compounds also showed a medium intense $\nu(\text{C}\equiv\text{N})$ stretching vibration, the position of which was influenced by substituents R^1-R^3 at the same extent as was the $\nu(\text{C}=\text{O})$ stretching vibration. Compounds *I*, *III*, *VI* and *XI* displayed the wave number difference 12 cm^{-1} , that of *II*, *IV*, *VIII* and *XVIII* was a little lower (9 cm^{-1}). The difference between compounds *VII* and *XII* was only 3 cm^{-1} , whereas *V* and *IX* revealed no difference.

The $\nu(\text{C}-\text{N})$ stretching vibration of medium intensity at $1370-1392\text{ cm}^{-1}$ was influenced by substituents R^1-R^3 . The symmetric stretching vibration $\nu_s(\text{C}-\text{O})$ was associated with an intense band in the $960-1037\text{ cm}^{-1}$ region, the $\nu(\text{C}-\text{C})$ stretching vibration of medium intensity with the band at $873-970\text{ cm}^{-1}$. The symmetric $\nu_s(\text{OPO})$ vibration of medium intensity appeared at $850-902\text{ cm}^{-1}$ in CHCl_3 , whilst in CCl_4 the differences were greater mainly when $\text{R}^2 = \text{Cl}$ and amounted up to 12 cm^{-1} with compounds *IX*, *XII*, *XVI*. The asymmetric vibration $\nu_{as}(\text{OPO})$ of medium intensity recorded in CHCl_3 only was seen in the $820-854\text{ cm}^{-1}$ region.

Stretching vibration $\nu_s(\text{C—O})$, $\nu(\text{C—C})$, $\nu_s(\text{OPO})$ and $\nu_{as}(\text{OPO})$ referred to 1,3,2-dioxaphospholane-2-thione or 1,3,2-dioxaphosphorinane-2-thione ring and their location was influenced only by substitution at position 4, 5 and 6 of those rings.

The UV spectra, of the synthesized compounds were characteristic of two maxima, the first of which in the 211–216 nm region was due to a $\pi \rightarrow \pi^*$ transition, the second one appeared at 284–309 nm excepting *XIV* and *XV* ($R^2 = \text{SC}_2\text{H}_5$ and SC_3H_7) having this maximum at 321 nm. The bathochromic shift can be rationalized by conjunction of sulfur into the conjugated system. The second maximum was assigned the $n \rightarrow \pi^*$ transition.

Pesticide effect in tests of contact and systemic insecticide activity towards *Musca domestica*, *Calandra granaria* and *Aphis fabae* and acaricide effect towards females of *Tetranychus urticae* could be neglected. The relatively highest values towards eggs of *T. urticae* displayed compounds *I*, *III*, *V*, *VII*, *XI–XIII* and *XVII* in a 0.5% concentration (100%), nonetheless only compound *XVII* had this effect more than 50% in a 0.05% concentration (53%). None of the tested compounds was effective in the first screening as a fungicide in such an extent as to be subjected to further precision tests. Values of pesticide efficacy let us conclude that incorporation of phosphorus into the heterocyclic system, *i.e.* formation of a 1,3,2-dioxaphospholane or 1,3,2-dioxaphosphorinane-2-thione ring resulted in a notable decrease of insecticide, acaricide and fungicide effects when compared with $\begin{matrix} \text{R}^1\text{O} \\ \text{R}^2\text{O} \end{matrix} \text{P}(\text{S})$ -substitution at phosphorus; the ovicide efficacy only was so-so preserved.

EXPERIMENTAL

Methods

IR spectra ($400\text{--}2200\text{ cm}^{-1}$) were recorded with an IR Specord 75 (Zeiss, Jena) apparatus, UV spectra with a Unicam SP 8000 spectrophotometer (calibrated with a holmium filter) in methanol in a $2 \cdot 10^{-5}\text{--}5 \cdot 10^{-5}\text{ M}$ solutions in 1 cm-cells.

Compounds

1-Alkyl, phenyl-5-alkoxy, alkylthio, chloro-6-oxo-1*H*-pyridazin-4-ols were prepared according to⁷, 2-chloro-1,3,2-dioxaphospholane-2-thione, 4,5-dimethyl-2-chloro-1,3,2-dioxaphospholane-2-thione, 6-methyl-2-chloro-1,3,2-dioxaphosphorinane-2-thione and 5,5-dimethyl-2-chloro-1,3,2-dioxaphosphorinane-2-thione according to⁸.

To sodium or potassium salt of 5-alkoxy, alkylthio, chloro-1-alkyl, phenyl-6-oxo-1*H*-pyridazin-4-ol (55 mmol) in acetone (100 ml) the corresponding 2-chloro-1,3,2-dioxaphospholane-2-thione or 2-chloro-1,3,2-dioxaphosphorinane-2-thione (50 mmol) was added and stirring was continued for 2–4 h at a reflux temperature. The cooled mixture was poured into the stirred water (30 ml), the separated solid was filtered off and purified by crystallization. If the product is liquid, it was extracted with toluene (100 ml), washed with water, 5% sodium carbonate, dried, toluene was removed and the residue purified by column chromatography according to⁵.

TABLE II
Spectral Data

Compound	IR Spectra, cm^{-1}						UV λ_{max} , nm (ϵ , log)	Solvent		
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}-\text{N})$	$\nu_s(\text{C}-\text{O})$	$\nu(\text{C}-\text{C})$	$\nu_s(\text{OPO})$			$\nu_{\text{as}}(\text{OPO})$	
<i>I</i>	1 647	1 617	1 381	1 032	927	882	835	213 (4-29)	284 (3-60)	CHCl_3
<i>II</i>	1 666	1 629	1 373	1 037	925	881	—	213	288	CCl_4
	1 650	1 628	1 380	1 034	927	882	850	(4-30)	(3-78)	CHCl_3
<i>III</i>	1 652	1 620	1 380	962	881	862	—	213	286	CCl_4
	1 645	1 620	1 381	964	885	857	821	(4-31)	(3-70)	CHCl_3
<i>IV</i>	1 665	1 627	1 367	960	893	850	—	214	296	CCl_4
	1 657	1 628	1 368	962	895	850	820	(4-30)	(3-70)	CHCl_3
<i>V</i>	1 684	1 613	1 392	961	896	872	—	212	302	CCl_4
	1 670	1 612	1 387	988	897	876	823	(4-26)	(3-71)	CHCl_3
<i>VI</i>	1 639	1 608	1 373	988	896	876	854	213 (4-30)	285 (3-72)	CHCl_3
	1 644	1 599	1 373	988	897	874	839	213 (4-32)	296 (3-68)	CHCl_3
<i>VIII</i>	1 649	1 620	1 372	987	945	896	833	212 (4-36)	297 (3-72)	CHCl_3
<i>IX</i>	1 685	1 612	1 387	983	968	890	—	212	309	CCl_4
	1 671	1 613	1 388	995	970	902	821	(4-17)	(3-70)	CHCl_3
<i>X</i>	1 646	1 598	1 383	998	876	851	827	211 (4-30)	292 (3-49)	CHCl_3

TABLE II
(Continued)

Compound	IR Spectra, cm^{-1}							UV λ_{max} , nm (ϵ , log)	Solvent	
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}-\text{N})$	$\nu_s(\text{C}-\text{O})$	$\nu(\text{C}-\text{C})$	$\nu_s(\text{OPO})$	$\nu_{\text{as}}(\text{OPO})$			
XI	1 645	1 618	1 380	1 007	884	858	832	212 (4.30)	285 (3.72)	CHCl_3
XII	1 678 1 652	1 602	1 383 1 384	1 050 1 048	883 887	867 850	834	212 (4.29)	294 (3.56)	CCl_4 CHCl_3
XIII	1 645	1 615	1 380	1 006	885	860	839	215 (4.26)	286 (3.64)	CHCl_3
XIV	1 636	1 580	1 376	1 007	883	850	835	212 (4.16)	321 (3.86)	CHCl_3
XV	1 645 1 636	1 579 1 580	1 373 1 372	1 006 1 007	883 882	856 855	— 832	212 (4.14)	321 (3.87)	CCl_4 CHCl_3
XVI	1 667 1 652	1 603 1 603	1 380 1 382	1 006 1 007	871 873	839 851	— 834	213 (4.34)	296 (3.61)	CCl_4 CHCl_3
XVII	1 639	1 620	1 373	1 008	880	857	832	215 (4.30)	287 (3.67)	CHCl_3
XVIII	1 653	1 625	1 370	1 007	878	854	836	216 (4.02)	296 (3.56)	CHCl_3

Pesticide Activity

The contact insecticide effect was investigated on *Musca domestica* L., *Calandra granaria* L. and *Aphis fabae* Scop. using metation (O,O-dimethyl-O-(3-methyl-4-nitrophenyl) thiophosphate) as a reference. The systemic insecticide activity was examined on *A. fabae* using Intration (O,O-diethyl-S-(2-ethylthioethyl) dithiophosphate) as a standard. The acaricide and ovicide effects were studied on *Tetranychus urticae* Koch. and eggs of *T. urticae*, respectively, employing Akarition (O,O-diethyl-S-(4-chlorophenylthiomethyl) dithiophosphate) as a reference. Procedures for determining the insecticide, acaricide and ovicide activities were already published^{9,10}. The fungicide effect was investigated on *Tilletia foetida*, *Botrytis cinerea* and *Fusarium nivale* by a zone method using Kaptan (3a,4,7,7a-tetrahydro-N-trichloromethanesulfenylphthalimide) as a standard. The antipowdery mildew activity was estimated by spraying the living barley subspecies Dunajský trh (*Erysiphe graminis* DC) using Chloraniformetan (1-(3,4-dichloroanilino)-1-formyl-amido-2,2,2-trichlorethane) as a reference, on cucumbers (*E. polyphaga* HAMMARLUND) using Dinocap (2,4-dinitro-6-octylphenyl crotonate and 2,6-dinitro-4-octylphenyl crotonate) as a standard and on tomatoes (*Phytophthora infestans* DE BY) by the spray-on method using Mankozeb (manganese and zinc ethylenebisdithiocarbamate in a 7 : 1 ratio) according to¹¹. The systemic activity towards *E. polyphaga* and *P. infestans* on cucumber and tomato plants, respectively, was estimated by watering according to⁹ employing Tridemorf (N-tridecyl-2,6-dimethylmorpholine) as a reference.

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