

Synthesis, spectral properties, and insecticidal, acaricidal, and ovicidal activities of some *O*-(2- R^4 -5- R^3 -3-oxo-2*H*-pyridazin-4-yl)phosphates and phosphorothioates

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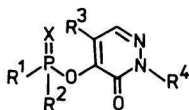
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A synthesis of 22 *O*-(2- R^4 -5- R^3 -3-oxo-2*H*-pyridazin-4-yl)phosphates and phosphorothioates is described. Infrared and ultraviolet spectra of the compounds prepared are interpreted. The contact and systemic insecticidal, acaricidal, and ovicidal activities of compounds synthesized were evaluated.

Описывается синтез 22 *O*-(2- R^4 -5- R^3 -оксо-2*H*-пиридазин-4-ил)фосфатов и тиофосфатов. Обсуждаются их ИК и УФ спектры и дана оценка их контактного и системного инсектицидного, акарицидного и овицидного действий.

Continuing the study of the relation between the chemical structure and pesticidal activity of pyridazin-4-yl organophosphoric acid esters we prepared a new group of pyridazin-4-yl organophosphoric and organothiophosphoric acid esters of the formula



Infrared and ultraviolet spectra of the prepared compounds *I*—*XXII* (Table 1) are interpreted and their contact and systemic insecticidal, acaricidal, and ovicidal activities are evaluated. The infrared and ultraviolet spectral data of compounds prepared are summarized in Table 2. Very strong bands, $\nu(\text{C}=\text{O})$ in the region 1635—1676 cm^{-1} were observed suggesting that the wavenumber of the band is influenced by the substituents. However, the wavenumber of the bands is not very influenced by the substituents R^1 and R^2 having alkoxy or alkylthio groups attached to the phosphorus atom, the wavenumber of the $\nu(\text{C}=\text{O})$ bands being observed in

Table 1

Physical data of compounds prepared

Compound	R ¹	R ²	R ³	R ⁴	X	Calculated/found			Yield %	M.p., °C <i>n</i> _D ²⁰
						% P	% N	% S		
I	CH ₃ O	CH ₃ O	CH ₃ O	CH ₃	O	11.7	10.6	—	62	135—136
						12.0	11.0			
II	C ₂ H ₅ O	C ₂ H ₅ O	CH ₃ O	CH ₃	O	10.6	9.6	—	63	86—87
						10.5	9.7			
III	CH ₃ O	(CH ₃) ₂ CHCH ₂ O	CH ₃ O	CH ₃	S	9.6	8.7	9.9	84	1.5080
						9.7	8.8	10.0		
IV	C ₂ H ₅ O	C ₂ H ₅ O	CH ₃ O	CH ₃	S	10.0	9.1	10.4	67	78—80
						9.9	9.3	10.6		
V	C ₂ H ₅ O	(CH ₃) ₂ CHO	CH ₃ O	CH ₃	S	9.6	8.7	9.9	66	73—75
						9.7	9.0	10.0		
VI	C ₃ H ₇ O	C ₃ H ₇ O	CH ₃ O	CH ₃	O	9.7	8.7	—	88	63—64
						9.8	8.9			
VII	(CH ₃) ₂ CHO	(CH ₃) ₂ CHO	CH ₃ O	CH ₃	S	9.2	8.3	9.5	20	96—98
						9.1	8.2	9.8		
VIII	C ₂ H ₅ S	(CH ₃) ₂ CHO	CH ₃ O	CH ₃	O	9.6	8.7	9.9	29	77—79
						9.4	8.9	10.0		
IX	C ₂ H ₅ O	(CH ₃) ₂ CHS	CH ₃ O	CH ₃	O	9.6	8.7	9.9	48	144—146
						9.5	8.6	10.1		
X	C ₂ H ₅ O	C ₃ H ₇ S	CH ₃ O	CH ₃	S	9.2	8.3	19.0	71	41—42
						9.3	8.3	19.1		

Table 1 (Continued)

Compound	R ¹	R ²	R ³	R ⁴	X	Calculated/found			Yield %	M.p., °C <i>n</i> _D ²⁰
						% P	% N	% S		
XI	CH ₃ O	(CH ₃) ₂ CHNH	CH ₃ O	CH ₃	S	10.1	13.7	10.4	49	75—77
						10.2	13.8	10.6		
XII	C ₂ H ₅ O	C ₂ H ₅ O	CH ₃ O	CH ₃	S	10.6	9.6	11.0	41	82—83
						10.5	9.7	11.1		
XIII	OCH(CH ₃)CH	(CH ₃) ₂ O	CH ₃ O	CH ₃	S	10.1	9.1	10.5	74	104—105
						10.2	9.3	10.6		
XIV	C ₂ H ₅ O	(CH ₃) ₂ CHO	CH ₃ O	C ₆ H ₅	S	8.1	7.3	8.3	52	88—89
						8.2	7.3	8.5		
XV	C ₂ H ₅ O	(CH ₃) ₂ CHO	CH ₃ O	C ₆ H ₁₁	S	8.0	7.2	8.2	49	76—77
						7.8	7.4	8.3		
XVI	C ₂ H ₅ O	(CH ₃) ₂ CHO	CH ₃ O	C ₆ H ₁₃	S	7.9	7.1	8.2	39	1.5079
						8.0	7.2	8.3		
XVII	C ₂ H ₅ O	(CH ₃) ₂ CHO	C ₂ H ₅ O	CH ₃	S	9.2	8.3	9.5	71	86—87
						9.1	8.4	9.5		
XVIII	CH ₃ O	C ₂ H ₅ O	C ₂ H ₅ O	CH ₃	S	10.1	9.1	10.5	68	119—121
						10.3	9.3	10.7		
XIX	C ₂ H ₅ O	(CH ₃) ₂ CHO	CH ₃ S	CH ₃	S	9.2	8.3	19.0	71	84—86
						9.0	8.4	18.8		
XX	C ₂ H ₅ O	(CH ₃) ₂ CHO	C ₂ H ₅ S	CH ₃	S	8.8	8.0	18.2	73	1.5382
						8.9	8.1	18.4		
XXI	(CH ₃) ₂ N	(CH ₃) ₂ N	C ₂ H ₅ S	CH ₃	O	9.7	17.5	10.0	58	74—76
						9.8	17.6	10.1		
XXII	C ₂ H ₅ O	(CH ₃) ₂ CHO	Cl	C ₆ H ₅	S	8.0	7.2	8.3	65	48—50
						8.2	7.4	8.5		

Table 2

Infrared and ultraviolet spectral data of compounds studied

Compound	$\tilde{\nu}/\text{cm}^{-1}$				$\lambda_{\text{max}}/\text{nm}$		
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}-\text{N})$	$\nu(\text{P}=\text{X})$	$\log \epsilon$		
<i>I</i>	1655	1630	1391	1277	216	292	
				1299	4.44	3.99	
<i>II</i>	1657	1631	1392	1277	212	257	288
				1300	4.48	3.66	3.73
<i>III</i>	1659	1624	1390	690	213	261	290
					4.50	3.58	3.74
<i>IV</i>	1660	1627	1391	691	213	261	289
					4.49	3.58	3.73
<i>V</i>	1656	1622	1388	685	213	266	289
					4.05	3.51	3.61
<i>VI</i>	1664	1631	1392	1277	213	260	290
				1296	4.41	3.55	3.73
<i>VII</i>	1658	1621	1390	688	213	260	290
					4.11	3.55	3.70
<i>VIII</i>	1661	1630	1391	1278	215		287
				1300	4.42		3.86
<i>IX</i>	1660	1631	1391	1277	216		286
				1300	4.50		4.05
<i>X</i>	1663	1625	1398	693	213	262	291
					4.42	3.63	3.69
<i>XI</i>	1635	1621	1379	684	213	266	288
					4.38	3.57	3.74
<i>XII</i>	1663	1627	1392	684	213	262	289
					4.45	3.62	3.71
<i>XIII</i>	1653	1624	1377	—	213	257	287
					4.38	3.51	3.64
<i>XIV</i>	1673	1643	1401	692	214	266	301
					4.47	3.87	3.83
<i>XV</i>	1651	1624	1388	694	213	260	292
					4.49	3.63	3.72
<i>XVI</i>	1667	1634	1388	686	214	261	290
				661	4.37	3.56	3.63
<i>XVII</i>	1663	1628	1388	660	213	260	289
					4.42	3.58	3.66
<i>XVIII</i>	1660	1630	1391	672	214	262	290
					4.46	3.61	3.72
<i>XIX</i>	1665	1607	1390	664	216	234	296
					4.11	3.81	3.75

Table 2 (Continued)

Compound	$\bar{\nu}/\text{cm}^{-1}$				$\lambda_{\text{max}}/\text{nm}$		
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}-\text{N})$	$\nu(\text{P}=\text{X})$		$\log \epsilon$	
XX	1664	1608	1386	662	215	236	294
					4.05	3.83	3.78
XXI	1662	1610	1388	1279	213	260	292
				1298	4.16	3.86	3.80
XXII	1676	1610	1384	689	212	262	306
					4.38	3.69	3.82

the region 1635—1667 cm^{-1} . The lowest wavenumber of the $\nu(\text{C}=\text{O})$ band was observed in the spectrum of compound XI, which could be explained by the presence of the intramolecular hydrogen bond between the N—H and the C=O groups.

The highest wavenumbers of the $\nu(\text{C}=\text{O})$ bands were observed in the spectra of compounds XIV and XXII, which is due to the presence of the phenyl group attached to the nitrogen atom of the pyridazinone ring.

The $\nu(\text{C}=\text{N})$ bands were observed in the spectra of compounds studied excepting compounds XIV, XIX—XXII in the region 1621—1631 cm^{-1} . The lowest wavenumber of the $\nu(\text{C}=\text{N})$ bands (1607—1610 cm^{-1}) was observed in the spectra of compounds XIX—XXII containing the sulfur or chlorine atoms attached to the carbon atom of the pyridazinone ring.

In the ultraviolet spectra of compounds studied (Table 3) two or three bands were observed of which the bands at the shortest wavelengths ($\lambda_{\text{max}} \sim 214 \text{ nm}$) can be assigned to the $\pi \rightarrow \pi^*$ transition and the position of these bands is almost not influenced by the nature of the substituents. The bands at the longest wavelengths ($n \rightarrow \pi^*$ transitions) were in the region 286—306 nm and λ_{max} of these bands was strongly dependent on the nature of the substituents.

By studying the insecticidal, acaricidal, and ovicidal activities of compounds studied one of the most active compounds, *O*-ethyl *O*-isopropyl *O*-(2-methyl-4-methoxy-3-oxo-1*H*-pyridazin-5-yl)phosphorothioate [1, 2] (compound XXIII), was included for comparison. The insecticidal activity of compounds V, VI, and XI against *M. domestica* was shown to be of the same order as that of compound XXIII, but significantly higher than that of Malathion and reached approximately the 50% value of Fenitrothion standard (Table 3). Compounds I, VIII, XII, and XVII were as active as the Malathion standard. None of the compounds was as active as the used standards against *S. granarius*. The contact insecticidal activity against *A. fabae* of compound V was on the same level with the used standards. None of the compounds was as active as compound XXIII and

Table 3

Insecticidal, acaricidal, and ovicidal activity (LC₅₀)^a of compounds prepared and of some standard pesticides

Compound	Contact activity					Systemic activity
	<i>Musca domestica</i>	<i>Sitophylus granarius</i>	<i>Aphis fabae</i>	<i>Tetranychus</i>	<i>urticae</i>	<i>Aphis fabae</i> Eggs
				Adults	Eggs	
I	230	+	820	26	++	480
II	710	780	250	5.6	720	500
III	750	840	480	28	650	820
IV	680	+	270	11	160	+
V	80	500	4.8	2.4	800	+
VI	84	+	+	+	++	+
VII	1100	+	880	310	1000	+
VIII	160	+	+	+	++	+
IX	++	+	+	+	++	+
X	2400	+	+	+	++	+
XI	85	+	750	+	1100	900
XII	260	+	12	680	160	500
XIII	++	+	+	+	100	+
XIV	++	+	+	+	+	+
XV	++	+	+	130	110	800
XVI	1000	+	+	16	120	940
XVII	120	880	+	+	++	+
XVIII	350	+	420	+	2400	+
XIX	++	+	+	+	++	+
XX	++	+	+	+	++	+
XXI	++	+	+	+	++	620
XXII	2600	+	620	360	++	+
XXIII ^b	52	60	0.88	0.22	240	+
Malathion	200	70	46	32	++	+
Fenitrothion	40	5.3	6.9	170	++	+
Karbofenthion	++	+	3.4	0.56	4.4	+
Thiometon	—	—	—	—	—	2.1

a) LC₅₀: concentration (mg l⁻¹) required to kill 50% of the test species; b) *O*-ethyl *O*-isopropyl *O*-(5-methoxy-1-methyl-6-oxo-1*H*-pyridazin-4-yl)phosphorothioate.

+ > 1000, ++ > 5000.

Karbofenthion standard. Compounds I–V and XVI were more active than Malathion standard. Ovicidal activity of compounds studied on eggs of *T. urticae* was lower than that of Karbofenthion standard, however, compounds IV, XII, XIII, XV, and XVI were more active than compound XXIII. Insecticidal activity of compounds I–III, XI, XII, XV, XVI, and XXI on *A. fabae* was higher than that of compound XXIII, but by two orders less than that of Thiometon standard.

The toxicity on rats per os was found to be lower with compound V ($LD_{50} = 25 \text{ mg kg}^{-1}$) than that with compound XXIII ($LD_{50} = 5.3 \text{ mg kg}^{-1}$).

Experimental

Substituted 3-oxo-2*H*-pyridazin-4-ols were prepared according to [3]. Dialkyl phosphorochloridoates, *O,O*-dialkyl phosphorochloridodithioates, *O,S*-dialkyl phosphorochloridodithioates, *O*-ethyl *S*-propyl phosphorochloridodithioate, *O*-methyl *N*-isopropylphosphorochloridoamidodithioate, *O*-ethyl ethylphosphonochloridodithioate, *N,N,N',N'*-tetramethylphosphorochloridoamide, and 4,5-dimethyl-2-chloro-1,3,2-dioxaphospholan-2-thione were prepared by the methods already described [4–8].

Infrared spectra were recorded with a UR-20 (Zeiss, Jena) instrument. The wavenumber calibration was checked against the spectrum of polystyrene. The spectra were recorded in carbon tetrachloride solution (concentration 20–60 mM, cell thickness 0.89 mm).

Ultraviolet spectra were recorded with a UV VIS (Zeiss, Jena) instrument in methanol (concentration 10–100 μM , cell thickness 10 mm). Analar carbon tetrachloride was purified according to a general procedure and spectral grade methanol was used.

The purity of compounds was controlled by thin-layer chromatography (on Silufol R with a UV 254 luminescence indicator or Silufol R without an indicator (Lachema, Brno)) using A. benzene + acetone (9 + 1 and 8 + 2) or B. petroleum ether + acetone (8 + 2 by volume) as developing agents. Detection was carried out by 0.5% light petroleum solution of 2,6-dibromo-*p*-benzoquinone chloroimine at 120°C as well as by ultraviolet light ($\lambda = 254 \text{ nm}$).

Column chromatography was performed on Silica gel L 93–149 μm (Lachema, Brno). Silica gel was activated for 6 h at 140°C before use. Toluene containing acetone (0–10% by volume) was used as eluting solvent. The separation of compounds was controlled by t.l.c.

Methods published previously [9, 10] were used to evaluate contact insecticidal activity against *Musca domestica*, *Sitophylus granarius*, and *Aphis fabae* using Malathion and Fenitrothion as standards, systemic aphicidal activity against *Aphis fabae* on *Chrysanthemum indicum* using Thiometon as standard, acaricidal activity against female *Tetranychus urticae* KOCH using Malathion, Fenitrothion, and Karbofenthion as standards and ovicidal activity against eggs of *T. urticae* using Karbofenthion as standard.

O-(2-*R*⁴-5-*R*³-3-oxo-2*H*-pyridazin-4-yl)phosphates and thiophosphates (I–XXII)

To a suspension of potassium salt of 2,5-disubstituted 3-oxo-2*H*-pyridazin-4-ol (0.11 mol) in acetonitrile (100 ml) and appropriate ester of phosphoric, phosphorothionic, and phosphonothionic acid (0.1 mol) was added with stirring at 15–20°C. Stirring was continued for 1–8 h at 40–80°C and then toluene (100 ml) was added, the reaction mixture was washed with water, aqueous sodium carbonate (5% solution) and again with water. After drying the product over anhydrous sodium sulfate the toluene was distilled off

under reduced pressure. The solid compounds were purified by crystallization and liquid compounds by column chromatography.

Chemical and physical properties of compounds prepared are summarized in Table 1.

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