Synthesis and pesticidal activity of some *O*,*O*-dialkyl *O*-(1-phenyl-6-oxo-1*H*-pyridazin-3-yl) thiophosphates

V. KONEČNÝ, Š. VARKONDA, and V. KUBALA

Research Institute of Agrochemical Technology,
810 04 Bratislava

Received 21 February 1978

The synthesis and pesticidal activity of some *O*,*O*-dialkyl *O*-(1-phenyl-6-oxo-1*H*-pyridazin-3-yl) thiophosphates is described. Some of the tested compounds were more active against *T. urticae* and its eggs as well as against *A. fabae* than the standard Ofunak. Against soil parasites not only the initial but also the residual activity of some compounds was higher than that of the above-mentioned standard.

Описывается синтез и пестицидная активность некоторых *O*,*O*-диалкил *O*-(1-фенил-6-оксо-1*H*-пиридазин-3-ил) тиофосфатов. Некоторые из исследованных соединений были более активные по отношению к *T. urticae* и ее личинкам и также к *A. fabae*, чем стандартный Ofunak. По отношению к почвенным паразитам не только исходная, но и остаточная активность некоторых соединений оказалась выше указанного стандарта.

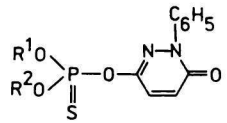
From numerous biologically tested phosphorus-containing organic compounds, 3-pyridazinyl organophosphates belong to that group which has been paid attention since the beginning of the 60th years. Great number of these compounds were synthesized and biologically tested [1—13]. From the above-mentioned group of compounds, *O*,*O*-diethyl *O*-(1-phenyl-6-oxo-1*H*-pyridazin-3-yl) thiophosphate, known as Ofunak (common name Pyridafention, produced by Sumitomo, Japan), has been used in practice as insecticide and nematocide. Ofunak belongs to the little toxic phosphorus-containing organic preparations ($LD_{50} = 780$ mg/kg p.o. on rats) and is designated mainly for extermination of soil parasites at cultivation of rice [14, 15]. It is also used in the mixture with Sumition [16]. The mechanism of its action in the soil was followed by labelled phosphorus [17] and the elaborated analytical procedure [18]. From the latest works the synthesis, which is rather difficult, of *O*-ethyl *S*-propyl *O*-(1,4,5-X-6-oxo-1*H*-pyridazin-3-yl) dithiophosphates is worth mentioning [19]. These compounds are active insecticides and their toxicity against haematothermal organisms is reduced.

In the present work we focused our attention to the synthesis of new 3-pyridazinyl thiophosphates (Table 1) of the formula

Table 1

Characterization of the synthesized compounds

Compound	R^1	R^2	Formula	M	Calculated/found % P	% N	% S	% Cl	Yield %	n_D^{20} (M.p., °C)
I	CH_3	C_2H_5	$C_{13}H_{15}N_2O_4PS$	326.30	9.50 9.35	8.59 8.90	9.83 9.58	—	69.1	1.2841
II	CH_3	C_3H_7	$C_{14}H_{17}N_2O_4PS$	340.32	9.10 8.93	8.23 8.47	9.42 9.26	—	70.2	1.5791
III	CH_3	$(CH_3)_2CH$	$C_{14}H_{17}N_2O_4PS$	340.32	9.10 8.93	8.23 8.47	9.42 9.26	—	70.8	1.5757
IV	CH_3	$(CH_3)_2CHCH_2$	$C_{15}H_{19}N_2O_4PS$	354.36	8.74 8.44	7.90 7.95	9.05 9.33	—	75.1	1.5651
V	CH_3	$ClCH_2CH_2$	$C_{13}H_{14}ClN_2O_4PS$	360.75	8.59 8.25	7.76 7.50	8.88 8.52	9.83 9.69	86.2	1.5870
VI	CH_3	$C_2H_5OCH_2CH_2$	$C_{15}H_{19}N_2O_5PS$	370.35	8.36 8.06	7.56 7.88	8.66 9.01	—	70.0	1.5806
VII	C_2H_5	C_3H_7	$C_{15}H_{19}N_2O_4PS$	354.36	8.74 9.01	7.90 7.82	9.05 9.37	—	89.1	(50—51)
VIII	C_2H_5	$(CH_3)_2CH$	$C_{15}H_{19}N_2O_4PS$	354.36	8.74 8.99	7.90 8.06	9.05 9.16	—	86.2	1.5691
IX	C_2H_5	$(CH_3)_2CHCH_2$	$C_{16}H_{21}N_2O_4PS$	368.38	8.41 8.77	7.60 7.85	8.70 9.01	—	87.5	1.5569
X	C_2H_5	$ClCH_2CH_2$	$C_{14}H_{16}ClN_2O_4PS$	374.78	8.26 8.56	7.47 7.41	8.56 8.65	9.46 9.68	70.0	1.5813
XI	C_2H_5	$C_2H_5OCH_2CH_2$	$C_{16}H_{21}N_2O_5PS$	384.38	8.06 7.85	7.29 7.54	8.34 7.98	—	80.1	1.5612
XII	C_2H_5	$CH\equiv C—CH_2$	$C_{15}H_{15}N_2O_4PS$	350.34	8.84 8.59	8.00 8.17	9.15 9.48	—	74.6	1.5826
XIII	C_3H_7	$(CH_3)_2CH$	$C_{16}H_{21}N_2O_4PS$	368.38	8.41 8.26	7.60 7.64	8.70 9.06	—	90.1	(64—65)
XIV	C_3H_7	$(CH_3)_2CHCH_2$	$C_{17}H_{23}N_2O_4PS$	382.41	8.10 7.90	7.33 7.40	8.68 8.61	—	78.7	1.5557
XV	C_3H_7	$ClCH_2CH_2$	$C_{15}H_{18}ClN_2O_4PS$	388.81	7.97 8.24	7.21 7.31	8.27 8.02	9.12 9.43	74.4	1.5745
XVI	C_3H_7	$C_2H_5OCH_2CH_2$	$C_{17}H_{23}N_2O_4PS$	398.11	7.77 7.42	7.03 7.23	8.05 8.35	—	84.2	1.5485
XVII	$(CH_3)_2CH$	$(CH_3)_2CHCH_2$	$C_{17}H_{23}N_2O_4PS$	382.41	8.10 8.33	7.33 7.42	8.38 8.72	—	91.6	1.5510
XVIII	$(CH_3)_2CH$	$ClCH_2CH_2$	$C_{15}H_{18}ClN_2O_4PS$	388.81	7.97 8.09	7.21 7.45	8.27 8.26	9.12 9.32	74.8	1.5817
XIX	$(CH_3)_2CH$	$C_2H_5OCH_2CH_2$	$C_{17}H_{23}N_2O_5PS$	398.41	7.77 7.95	7.03 7.37	8.05 8.35	—	84.4	1.5520
XX	$(CH_3)_2CH$	$CH\equiv C—CH_2$	$C_{16}H_{17}N_2O_4PS$	364.36	8.50 8.80	7.79 8.15	8.80 9.02	—	79.8	1.5730



where R^1 = alkyl group; R^2 = alkyl group (propyn-2-yl, 2-chloroethyl, and 2-ethoxyethyl) with purpose to test them for insecticidal, acaricidal, ovicidal, and fungicidal activities as well as against soil parasites. We started from the materials available on the compound Ofunak which is economically advantageous and can be easily synthesized. We synthesized the above-mentioned group of compounds structurally very similar to the preparation Ofunak, used in biological tests as standard.

The synthesis was carried out by the reaction of esters of chlorothiophosphoric acid with potassium salt of 1-phenyl-6-oxo-1*H*-pyridazin-3-ol in acetonitrile at the boiling temperature of the reaction mixture for 2—6 h. The purity of the obtained products was followed by thin-layer chromatography. When necessary, the compounds were purified by column chromatography.

The contact insecticidal activity on *M. domestica* and *C. granaria*, the systemic insecticidal activity on *M. sanborni*, and the fungicidal activity of the prepared compounds as well as that of the standard Ofunak were low, consequently, they were not chosen for further precise experiments. The compounds *I* and *VIII* were

Table 2

Insecticidal, acaricidal, and ovicidal activity of the synthesized compounds

Compound	Contact toxicity (%)		
	Aphis fabae	*Tetranychus urticae*	
		Adults	Eggs
I	0.032	0.0012	0.19
II	>0.1	0.038	0.18
III	>0.1	0.032	0.271
IV	>0.1	0.044	>0.5
V	>0.1	0.045	0.50
VI	>0.1	0.054	>0.5
VII	>0.1	0.00065	0.0016
VIII	0.038	0.0017	0.19
IX	>0.1	0.048	0.27
X	>0.1	0.043	0.023
XII	>0.1	0.053	>0.5
XIII	>0.1	>0.1	0.25
Ofunak	0.043	0.0022	0.12

in contact insecticidal activity on *A. fabae* somewhat more active than the used standard. Better results were obtained on *T. urticae* where the compounds *I* and *VIII* were more active and the compound *VII* was far more active than Ofunak. Similarly in ovicidal activity on eggs of *T. urticae* several compounds showed higher activities than the standard Ofunak; the compound *VII* was twice more active. The results of tests are presented in Table 2.

Ofunak is used mainly as a soil insecticide and nematocide, *i.e.* against soil parasites usually at cultivation of rice. Therefore, we wanted to test this preparation against the soil parasites at our conditions simultaneously with the two mostly active compounds *I* and *VIII*. The initial and the residual activities against *Agriotes sp.* were determined. Both the tested compounds equalled Ofunak in the initial and the residual activities; the activity of the compound *I* was even higher (Table 3).

On the basis of the obtained results we came to the conclusion that none of the synthesized compounds will be utilized in practice in spite of the fact that the compound *VII* showed much higher acaricidal and ovicidal activity than the standard Ofunak. A great disadvantage of the compound *VII* is its high acute toxicity on rats p.o. $LD_{50} = 30—40$ mg/kg. We found also Ofunak to be little effective as a soil insecticide at our conditions and it could not be compared with the preparations used in our country for this purpose.

Table 3

Initial and residual actions on *Agriotes sp.*

Compound	Dose p.p.m.	LD_{50} (%)	
		Initial action 2 days	Residual action 2 weeks
I	3	67	50
	6	75	50
	12	87	70
VIII	3	35	20
	6	56	40
	12	75	55
Ofunak	3	45	30
	6	50	35
	12	55	50
Pyridation[a]	3	80	100
	6	100	100
	12	100	100

a) *O*-Ethyl *O*-isopropyl *O*-(5-methoxy-1-methyl-6-oxo-1*H*-pyridazin-4-yl) thiophosphate.

Experimental

Physical constants and data on elemental analysis of the synthesized compounds are summarized in Table 1.

Thin-layer chromatography was performed on Silufol "R" plates without indicator (Lachema, Brno) in the system benzene—acetone (9 : 1); the compounds were detected with 0.5% DQC (2,6-dibromoquinone 4-chloroimine) in petroleum ether at 120°C. Column chromatography was accomplished on Silica gel 100/160 mesh (Lachema, Brno) activated before use for 6 h at 140°C. Benzene with the addition of acetone (0—1% according to the nature of the impurities present) was used as eluting agent. The separation was checked by t.l.c.

Contact insecticidal activity was followed on *Musca domestica* L., *Calandra granaria* L., and *Aphis fabae* SCOP using Ofunak (*O*,*O*-diethyl *O*-(1-phenyl-6-oxo-1*H*-pyridazin-3-yl) thiophosphate) as standard. Systemic insecticidal activity was followed on *Macrosiphoniella sanborni* L. (host plant *Chrysanthemum indicum*). Acaricidal activity was followed on females of *Tetranychus urticae* KOCH, ovicidal activity on eggs of *T. urticae* using Ofunak as standard. The methods of tests for insecticidal, acaricidal, and ovicidal activities were published earlier [20, 21].

The initial and residual activity against the soil parasites (*Agriotes sp.*) was followed by the method described in [22] using Ofunak as standard.

Fungicidal activity was determined by the *in vitro* and *in vivo* methods. The inherent activity was followed by the glass slide method after Sharvell on spores of fungi *Sclerotinia fructicola* (WINT.) and *Fusarium nivale* (FR.) using Kaptan (3a,4,7,7a-tetrahydro-*N*-(trichloromethanesulfenyl) phthalimide) as standard. The antipowdery mildew activity was followed on the living plants of spring barley, sort Dunajský trh (*Erysiphe graminis* DC. and *Erysiphe cichoriacearum*), on cucumbers (*Erysiphe polyphaga*), and on tomatoes (*Phytophthora infestans* De BY using Dinokap (2,4-dinitro-6-octylphenyl crotonate) as standard. The methods of tests for fungicidal activity have already been published [20].

3-Pyridazinyl thiophosphates (I—XX)

To potassium salt of 1-phenyl-6-oxo-1*H*-pyridazin-3-ol (0.08 mol) in acetonitrile (100 ml), ester of chlorothiophosphoric acid (0.075 mol) was added at 18°C under stirring. The reaction mixture was stirred at the boiling temperature for 2—6 h. Toluene (100 ml) was added after cooling and the mixture was washed with water, 5% sodium carbonate, and water. Then it was dried over anhydrous sodium sulfate and toluene was distilled off under reduced pressure. The solid residue was purified by crystallization from petroleum ether. If necessary, the liquid residue was purified by column chromatography.

References

1. Du Breuil, S., *U.S.* 2759937 (1955).
2. Du Breuil, S., *J. Org. Chem.* ***26,*** 3382 (1961).
3. Österreichische Stickstoffwerke Akt., *Fr.* 1471951 (1967).

4. Bayer, A. G., *Swiss* 507304 (1971).
5. Rigterink, R. H., *U.S.* 3100206 (1963).
6. Teruhiko, T. *et al., Japan. Kokai* 10237 (1973); *Chem. Abstr.* ***79,*** 1372 (1973).
7. Makoto, N. *et al., Japan.* 12702 (1974); *Chem. Abstr.* ***82,*** 107550 (1975).
8. Mitsui Toatsu Chem. Ltd., *Japan.* 4858144; Ref. *CPI* V/5, p. 2 (1974).
9. Mitsui Toatsu Chem. Ltd., *Japan.* 008548; Ref. *CPI* W/23, p. 2 (1973).
10. Sankyo Co. Ltd., *Japan.* 19294 (1963); Ref. *Jap. Pat. Rep.* ***2*** (38), 5/10 (1963).
11. Schoenbeck, R. *et al., U.S.* 3310560; *Chem. Abstr.* ***67,*** 90825 (1967).
12. Österreichische Stickstoffwerke Akt., *Austrian* 252950; *Chem. Abstr.* ***67,*** 11497 (1967).
13. Mitsui Toatsu Chem. Inc., *Japan.* 12972 (1973).
14. Mizutani, K. *et al., Eisei Dobutsu* ***26*** (2—3), 145 (1975); *Chem. Abstr.* ***86,*** 51509 (1977).
15. Mitsui Toatsu Chem. Inc., *Japan.* 76014-568; Ref. *CPI* X/23, p. 1 (1976).
16. Chu Yan-I. *et al., Chih Wu Dao Hu Hsueh Hui Hui K'an* ***18*** (4) 377 (1976); *Chem. Abstr.* ***87,*** 146672 (1977).
17. Takatoshi, U. *et al., Noyaku Kagaku* ***1974,*** 159; *Chem. Abstr.* ***82,*** 39452 (1975).
18. Tetsuo, M., *Noyaku Kagaku* ***1974,*** 112; *Chem. Abstr.* ***82,*** 119947 (1975).
19. Bayer, A. G., *Ger. Offen* 2343741 (1973).
20. Demečko, J. and Konečný, V., *Agrochémia* (Bratislava) ***10,*** 127 (1970).
21. Drábek, J., Pastorek, I., and Konečný, V., *J. Sci. Food Agr.* ***20,*** 152 (1969).
22. Konečný, V., Varkonda, Š., Gehér, S., and Steskal, R., *Agrochémia* (Bratislava) ***17,*** 207 (1977).

Translated by A. Kardošová