# Synthesis and pesticidal activity of 2,4-disubstituted *O*-(haloalkyl)-*O*-(alkyl, aryl)-(*N*-alkylamido, *N,N*-dialkylamido)-*O*-(3-oxo-2*H*-pyridazine-5-yl) esters of thiophosphoric acid

[a]J. ŽÚŽIOVÁ, [a]V. KONEČNÝ, [b]Š. KOVÁČ, [a]Š. VARKONDA, and [c]B. ŽÚŽI

[a]*Research Institute of Chemical Technology, CS-831 06 Bratislava*

[b]*Department of Organic Chemistry, Faculty of Chemical Technology, Slovak Technical University, CS-812 37 Bratislava*

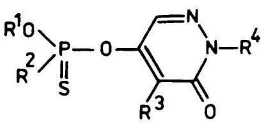
[c]*Department of Petroleum Chemistry and Technology, Faculty of Chemical Technology, Slovak Technical University, CS-812 37 Bratislava*

Received 19 February 1987

Synthesis of 2,4-disubstituted *O*-(haloalkyl)-*O*-(alkyl, aryl)-(*N*-alkylamido, *N,N*-dialkylamido)-*O*-(3-oxo-2*H*-pyridazine-5-yl) esters of thiophosphoric acid is described. Interpretation of infrared, ultraviolet, and NMR spectra is given together with the measurement of partition coefficients and dipole moments.

Описан синтез 2,4-дизамещенных *O*-(галоалкил)-*O*-(алкил, арил)-(*N*-алкиламидо, *N,N*-диалкиламидо)-*O*-(3-оксо-2*H*-пиридазин-5-ил)-овых эфиров тиофосфорной кислоты. Приводится интерпретация ИК-, УФ- и ЯМР-спектров данных соединений, а также результаты измерения коэффициентов разделения и дипольных моментов.

Organophosphorus compounds based on pyridazine and pyridazinone have received considerable attention for several years because many of them have demonstrated excellent pesticidal activities [1]. The method of preparation and the biological activity of some pyridazine-5-yl esters of thiophosphoric acid are published in the literature [2—7]. In a search for new pesticides a novel group of 2,4-disubstituted *O*-(haloalkyl)-*O*-(alkyl, aryl)-(*N*-alkylamido, *N,N*-dialkylamido)-*O*-(3-oxo-2*H*-pyridazine-5-yl) esters of thiophosphoric acid of the following general formula has been synthesized



*I–XXXVII*

The structure of compounds prepared was proved by spectral methods. In addition, partition coefficients and dipole moments of compounds prepared were measured.

*Table 1*

Characterization of the compounds prepared

| Compound | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Formula $M_r$ | $w_i$(calc.)/% $w_i$(found)/% P | S | N | Cl | Yield % | $n(\lambda_D, 20\,°C)$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *I* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3S$ | $CH_3$ | $C_{12}H_{20}ClN_2O_4PS_2$ | 8.00 | 16.58 | 7.24 | 9.16 | 83 | 1.5576 |
| | | | | | 386.68 | 7.91 | 16.84 | 7.13 | 8.88 | | |
| *II* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $C_5H_{11}$ | $C_{16}H_{28}ClN_2O_5PS$ | 7.25 | 7.51 | 6.56 | 8.30 | 85 | 1.5121 |
| | | | | | 426.65 | 7.08 | 7.24 | 6.75 | 8.49 | | |
| *III* | $ClCH_2CH_2$ | $C_2H_5O$ | Cl | $C_6H_5$ | $C_{14}H_{15}Cl_2N_2O_4PS$ | 7.57 | 7.84 | 6.84 | 17.33 | 75 | 1.5497 |
| | | | | | 409.07 | 7.64 | 8.21 | 7.05 | 17.68 | | |
| *IV* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $CH_3$ | $C_{11}H_{17}Cl_2N_2O_4PS$ | 8.26 | 8.54 | 7.47 | 18.89 | 81 | 1.5361 |
| | | | | | 375.07 | 8.49 | 9.21 | 7.63 | 18.69 | | |
| *V* | $ClCH_2CH_2$ | $(C_2H_5)_2N$ | $CH_3O$ | $CH_3$ | $C_{12}H_{21}ClN_3O_4PS$ | 8.37 | 8.67 | 11.36 | 9.59 | 90 | 1.5380 |
| | | | | | 369.68 | 8.83 | 9.27 | 11.09 | 9.86 | | |
| *VI* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $C_2H_5O$ | $C_6H_5$ | $C_{18}H_{24}ClN_2O_5PS$ | 6.93 | 7.17 | 6.27 | 7.93 | 78 | 1.5583 |
| | | | | | 446.68 | 7.22 | 6.88 | 6.69 | 8.16 | | |
| *VII* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $C_3H_7$ | $C_{13}H_{21}Cl_2N_2O_4PS$ | 7.68 | 7.95 | 6.94 | 17.59 | 76 | 1.5291 |
| | | | | | 403.06 | 7.68 | 7.86 | 7.15 | 17.60 | | |
| *VIII* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_2C_6H_5$ | $C_{18}H_{24}ClN_2O_5PS$ | 6.93 | 7.18 | 6.27 | 7.94 | 74 | 1.5534 |
| | | | | | 446.70 | 6.58 | 7.76 | 6.34 | 7.37 | | |
| *IX* | $ClCH_2CH_2$ | $CH_3O$ | $CH_3O$ | $CH_3$ | $C_9H_{14}ClN_2O_5PS$ | 9.42 | 9.76 | 8.52 | 10.79 | 66 | 1.5404 |
| | | | | | 328.65 | 9.14 | 10.08 | 8.01 | 10.75 | | |
| *X* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $C_2H_5O$ | $C_5H_{11}$ | $C_{17}H_{30}ClN_2O_5PS$ | 7.03 | 7.27 | 6.35 | 8.04 | 80 | 1.5111 |
| | | | | | 440.67 | 6.63 | 7.05 | 6.45 | 8.29 | | |
| *XI* | $ClCH_2CH_2$ | $C_2H_5O$ | $CH_3O$ | $C_6H_5$ | $C_{15}H_{18}ClN_2O_5PS$ | 7.65 | 7.92 | 6.92 | 8.76 | 74 | 1.5763 |
| | | | | | 404.60 | 7.64 | 8.21 | 7.05 | 8.68 | | |
| *XII* | $ClCH_2CH_2$ | $C_4H_9NH$ | $CH_3O$ | $CH_3$ | $C_{12}H_{21}ClN_3O_4PS$ | 8.37 | 8.67 | 11.36 | 9.59 | 89 | 1.5436 |
| | | | | | 369.63 | 8.15 | 9.48 | 11.39 | 9.44 | | |
| *XIII* | $ClCH_2CH_2$ | i-$C_5H_{11}O$ | $CH_3O$ | $CH_3$ | $C_{13}H_{22}ClN_2O_5PS$ | 8.05 | 8.33 | 7.28 | 9.22 | 78 | 1.5234 |
| | | | | | 384.66 | 7.74 | 8.86 | 7.48 | 9.38 | | |

Chem. Papers 42 (3) 415—427 (1988)



*Table 1* (Continued)

| Compound | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Formula $M_r$ | $w_i$(calc.)/% $w_i$(found)/% P | S | N | Cl | Yield % | $n(\lambda_D$, 20 °C) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *XIV* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{12}H_{20}ClN_2O_5PS$ | 8.35 | 8.65 | 7.55 | 9.56 | 70 | 1.5267 |
| | | | | | 370.62 | 8.15 | 8.62 | 7.95 | 9.66 | | |
| *XV* | $ClCH_2CH_2$ | $C_2H_5O$ | $CH_3O$ | $CH_3$ | $C_{10}H_{16}ClN_2O_5PS$ | 9.04 | 9.36 | 8.17 | 10.34 | 69 | 1.5360 |
| | | | | | 342.58 | 8.82 | 9.56 | 8.12 | 10.24 | | |
| *XVI* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3S$ | $C_6H_5$ | $C_{17}H_{22}ClN_2O_4PS_2$ | 6.90 | 14.29 | 6.24 | 7.90 | 65 | M.p. |
| | | | | | 448.72 | 6.98 | 14.55 | 6.41 | 8.12 | | 72.5—73 °C* |
| *XVII* | $ClCH_2CH_2$ | i-$C_4H_9NH$ | $CH_3O$ | $CH_3$ | $C_{12}H_{21}ClN_3O_4PS$ | 8.38 | 8.67 | 11.36 | 9.69 | 86 | 1.5407 |
| | | | | | 369.61 | 8.12 | 8.99 | 10.75 | 9.36 | | |
| *XVIII* | $ClCH_2CH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{13}H_{22}ClN_2O_5PS$ | 8.05 | 8.33 | 7.27 | 9.21 | 55 | 1.5231 |
| | | | | | 384.72 | 8.25 | 8.88 | 7.81 | 9.55 | | |
| *XIX* | $ClCH_2CH_2$ | i-$C_3H_7O$ | $CH_3O$ | $CH_3$ | $C_{11}H_{18}ClN_2O_5PS$ | 8.68 | 8.99 | 7.84 | 9.93 | 80 | 1.5280 |
| | | | | | 356.70 | 8.68 | 9.07 | 8.06 | 9.90 | | |
| *XX* | $ClCH_2CH_2$ | n-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{12}H_{20}ClN_2O_5PS$ | 8.35 | 8.65 | 7.55 | 9.56 | 45 | 1.5274 |
| | | | | | 370.66 | 8.19 | 8.49 | 7.65 | 10.50 | | |
| *XXI* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $C_6H_{11}$ | $C_{17}H_{28}ClN_2O_5PS$ | 7.05 | 7.30 | 6.38 | 8.09 | 77 | 1.5290 |
| | | | | | 438.67 | 7.19 | 7.09 | 6.63 | 8.67 | | |
| *XXII* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $C_4H_9$ | $C_{15}H_{26}ClN_2O_5PS$ | 7.50 | 7.76 | 6.78 | 8.59 | 91 | 1.5100 |
| | | | | | 412.65 | 7.25 | 7.47 | 6.45 | 8.88 | | |
| *XXIII* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $CH_2C_6H_5$ | $C_{17}H_{21}Cl_2N_2O_4PS$ | 6.87 | 7.10 | 6.20 | 15.71 | 78 | 1.5637 |
| | | | | | 451.12 | 6.67 | 6.95 | 6.01 | 15.87 | | |
| *XXIV* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | 3-$CF_3C_6H_4$ | $C_{17}H_{18}Cl_2F_3N_2O_4PS$ | 6.13 | 6.35 | 5.54 | 14.03 | 52 | 1.5419 |
| | | | | | 505.12 | 6.26 | 7.20 | 5.64 | 14.51 | | |
| *XXV* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $CH_2CH{=}CH_2$ | $C_{13}H_{19}Cl_2N_2O_4PS$ | 7.72 | 7.99 | 6.98 | 17.67 | 74 | 1.5373 |
| | | | | | 401.08 | 7.43 | 8.18 | 6.79 | 17.76 | | |
| *XXVI* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{12}H_{20}ClN_2O_5PS$ | 8.36 | 8.65 | 7.56 | 9.56 | 83 | 1.5255 |
| | | | | | 370.68 | 8.30 | 8.51 | 7.52 | 9.30 | | |

* Crystallized from cyclohexane.

*Table 1* (Continued)

| Compound | $R^1$ | $R^2$ | $R^3$ | $R^4$ | Formula $M_r$ | $w_i$(calc.)/% $w_i$(found)/% | | | | Yield | $n(\lambda_D, 20\,°C)$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | P | S | N | Cl | % | |
| *XXVII* | $ClCH_2CH_2$ | $C_6H_5O$ | $CH_3O$ | $CH_3$ | $C_{14}H_{16}ClN_2O_5PS$ | 7.92 | 8.20 | 7.16 | 9.07 | 94 | 1.5716 |
| | | | | | 390.72 | 7.50 | 8.05 | 7.21 | 9.16 | | |
| *XXVIII* | $ClCH_2CH_2$ | n-$C_3H_7O$ | $CH_3O$ | $CH_3$ | $C_{11}H_{18}ClN_2O_5PS$ | 8.68 | 8.99 | 7.84 | 9.94 | 70 | 1.5309 |
| | | | | | 356.70 | 9.08 | 9.74 | 7.73 | 9.97 | | |
| *XXIX* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $C_2H_5S$ | $CH_3$ | $C_{13}H_{22}ClN_2O_4PS_2$ | 7.73 | 16.00 | 6.98 | 8.85 | 79 | 1.5515 |
| | | | | | 400.67 | 7.88 | 15.55 | 6.67 | 9.80 | | |
| *XXX* | $FCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{12}H_{20}FN_2O_5PS$ | 8.74 | 9.05 | 7.90 | — | 64 | 1.5116 |
| | | | | | 354.22 | 8.60 | 9.10 | 7.80 | | | |
| *XXXI* | $BrCH_2CH_2$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{12}H_{20}BrN_2O_5PS$ | 7.46 | 7.72 | 6.74 | | 70 | 1.5362 |
| | | | | | 415.15 | 7.49 | 7.77 | 6.76 | | | |
| *XXXII* | $ClCH_2(CH_3)CH$ | i-$C_4H_9O$ | $CH_3O$ | $CH_3$ | $C_{13}H_{22}ClN_2O_5PS$ | 8.05 | 8.33 | 7.27 | 9.21 | 67 | 1.5217 |
| | | | | | 384.72 | 8.13 | 8.85 | 7.13 | 9.39 | | |
| *XXXIII* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $C_6H_{11}$ | $C_{16}H_{25}Cl_2N_2O_4PS$ | 6.98 | 7.24 | 6.32 | 16.00 | 80 | 1.5395 |
| | | | | | 443.10 | 6.83 | 7.65 | 6.66 | 15.46 | | |
| *XXXIV* | $ClCH_2CH_2$ | i-$C_4H_9O$ | $C_2H_5S$ | $C_2H_5$ | $C_{14}H_{24}ClN_2O_4PS_2$ | 7.46 | 15.46 | 6.75 | 8.55 | 86 | 1.5457 |
| | | | | | 414.70 | 7.97 | 15.52 | 6.75 | 8.94 | | |
| *XXXV* | $ClCH_2CH_2$ | $C_2H_5O$ | Cl | $CH_3$ | $C_9H_{13}Cl_2N_2O_4PS$ | 8.92 | 9.24 | 8.06 | 20.42 | 68 | 1.5497 |
| | | | | | 347.06 | 8.58 | 10.35 | 7.99 | 20.24 | | |
| *XXXVI* | $ClCH_2CH_2$ | i-$C_4H_9O$ | Cl | $C_4H_9$ | $C_{14}H_{23}Cl_2N_2O_4PS$ | 7.43 | 7.65 | 6.70 | 17.20 | 45 | 1.5259 |
| | | | | | 417.10 | 6.89 | 8.13 | 6.58 | 17.10 | | |
| *XXXVII* | $ClCH_2CH_2$ | $C_2H_5O$ | $C_2H_5S$ | $CH_2C_6H_5$ | $C_{17}H_{22}ClN_2O_4PS_2$ | 6.90 | 14.29 | 6.24 | 7.90 | 61 | 1.5848 |
| | | | | | 448.72 | 6.75 | 14.07 | 6.20 | 8.05 | | |

Characterization of compounds prepared is presented in Table 1. The preparation of compounds was carried out after procedures *A* and *B* described in the literature [5, 8]. A majority of compounds was prepared according to the procedure *A* because this procedure appeared to be simple and relatively suitable and afforded 80—95 % yields. However, the yields of compounds *V*, *VI*, *XIX*, *XXVI*, and *XXXVI* were low and they were not improved even if the temperature over 80 °C and the prolonged 8—10 h reaction time were used. Under these conditions more by-products were formed. It has been found that sodium or potassium salts of some 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ols are slightly soluble in organic solvents, *e.g.* 2-butanone, propanone, acetonitrile, dioxan, dimethylformamide and others used in reactions. This procedure has the disadvantage that in the heterogeneous system solid—liquid the reactions proceed slowly because a number of active collisions of the reacting molecules was significantly decreased which in turn reflected in the yields. The procedure *B* solved the disadvantage of the procedure *A* in such a way that the reactions were carried out in two-phase system organic solvent—water, in our case, toluene—water in the presence of the phase-transfer catalysts — quaternary ammonium salts (benzyltriethylammonium chloride, tetraethylammonium chloride, tetrabutylammonium bromide, *N*-ethyl-*N*-dodecylmorpholinium chloride, *N*-(2-bromoethyl)-*N*-methylpyrrolidinium bromide, cyclohexyldodecylammonium bromide and others). It can be assumed that in the aqueous phase a rapid equilibrium exchange of the cation of the appropriate salt of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol for the cation of the quaternary ammonium salt occurs followed by a transport of the formed ionic pair into the organic phase where the inherent reaction takes place. By the procedure *B* it was possible to synthesize compounds which after the procedure *A* form with difficulties and in low yields.

Tetrabutylammonium bromide was found to be the most suitable catalyst. The reactions were carried out under very mild conditions in the temperature range 20—70 °C and, in contrast to procedure *A*, the reaction time was shortened by a half. The yields and the purity of products were significantly raised. An interesting knowledge was obtained from the reaction of sodium salt of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol with an appropriate chlorothiophosphate in the absence of alkaline carbonate according to the procedure *B*. The reaction under these conditions did not afford a desirable product and by a prolonged reaction time and at higher temperature a mixture of several compounds was formed. This fact can be explained by that the reacting anion of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol was highly solvated because in the reaction system the amount of any salt was not sufficient to decrease the transport of water which can participate in solvation. The shielding effect of the solvate cage in surroundings of the reacting anion was probably so large that the reaction proceeded very slowly.

Spectral data of compounds prepared are given in Table 2. The ν(C=O) bands are observed in the region of $\tilde{\nu} = 1655$—$1689\ \text{cm}^{-1}$ (in tetrachloromethane). On passing from tetrachloromethane to trichloromethane solution the ν(C=O) bands are observed at lower wavenumbers by $\approx 15\ \text{cm}^{-1}$. The highest wavenumbers of the ν(C=O) bands $\tilde{\nu} = 1670$—$1689\ \text{cm}^{-1}$ are observed in the spectra of compounds *IV*, *VII*, *XXIII*—*XXV*, and *XXXV* where $R^3$ = Cl and $R^4$ = methyl, propyl, allyl, benzyl, 3-fluoromethylphenyl which is mainly due to the $-I$ effect and the field effect of the chlorine atom in the position 3 of the pyridazinone ring. The ν(C=N) bands of the compounds studied are observed in the region of $\tilde{\nu} = 1576$—$1629\ \text{cm}^{-1}$ (in tetrachloromethane). The wavenumbers of these bands are influenced by the nature of the $R^3$ substituents. The lowest wavenumbers ($\tilde{\nu} = 1576$—$1585\ \text{cm}^{-1}$) of the ν(C=N) bands are observed in the spectra of compounds having $R^3$ = methylthio and ethylthio groups (compounds *I*, *XVI*, *XXIX*, *XXXIV*, and *XXXVII*). The wavenumbers of the ν(P—O—$C_{aliph}$) bands are relatively constant, only with compounds *XIII* and *XIV* having a branched hydrocarbon chain a decrease of the wavenumbers of the ν(P—O—C) bands is observed. The ν(P=S) bands in the spectra of compounds studied are observed in the region of $\tilde{\nu} = 657$—$680\ \text{cm}^{-1}$.

In the ultraviolet spectra of compounds studied two absorption bands are observed in the region of $\lambda = 209$—$325$ nm (Table 2), the $\lambda_{max}$ of these bands is only slightly influenced by the nature of the substituents.

Chemical shifts of the carbons of the pyridazinone ring are only slightly influenced by the nature of the substituents, lower chemical shifts are observed in the spectra of compounds *III*, *IV*, *XXIII*—*XXV*, *XXIX*, *XXXIII*—*XXXVII* in which the chlorine atom or alkylthio group is attached to the carbon atom in the position 4 of the pyridazinone ring.

The $^{13}$P NMR spectra of compounds studied point out that the length of the hydrocarbon chain does not influence the chemical shift of the phosphorus atom. The highest chemical shifts of the phosphorus atom were observed in the spectra of compounds *V* and *XVII* (phosphorus atom attached to the alkylamido and dialkylamido groups). The lowest chemical shift of the phosphorus atom was observed in the spectrum of compound *XXVII* (phosphorus attached to the phenoxy group).

Dipole moments $\mu$ as well as partition coefficients $x$ depend on the nature of the substituents attached to the pyridazinone ring.

The determined values of the pesticidal activity of compounds studied are given in Table 3. It was found that the test compounds were ineffective against *Musca domestica* L. and *Sitophylus granarius*. A similar result was obtained in systemic tests on *Aphis fabae*. A good insecticidal activity against *Aphis fabae*

*Table 2*

Dipole moments $\mu$, ultraviolet, infrared, and NMR spectral data of compounds prepared

| Compound | $\frac{\mu}{10^{-30}\,\mathrm{C\,m}}$ | $\log x$ | $\lambda_{max}$/nm $\log(\varepsilon/(\mathrm{m^2\,mol^{-1}}))$ | | $\tilde{\nu}/\mathrm{cm^{-1}}$ ($CHCl_3/CCl_4$) ν(P=S) | ν(P—O—$C_{aliph}$) | ν(C=N) | ν(C=O) | $\delta$/ppm $^{13}$C-6 | $^{13}$C-5 | $^{13}$C-4 | $^{13}$C-3 | $^{31}$P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *I* | 10.83 | 3.97 | 211.0 | 321.0 | 649, 699 | 1011 | 1577 | 1640 | 131.63 | 148.66 | 129.03 | 160.22 | 62.06 |
| | | | 3.17 | 2.88 | 667, 721 | 1020 | 1581 | 1651 | | | | | |
| *II* | 9.86 | 5.30 | 214.0 | 287.5 | 654, 725 | 1018 | 1621 | 1647 | 133.97 | 144.89 | 138.20 | 158.92 | 63.39 |
| | | | 3.28 | 2.70 | 655, 721 | 1023 | 1625 | 1662 | | | | | |
| *III* | 12.56 | 2.65 | 211.0 | 308.0 | 655, 687 | 1024 | 1609 | 1674 | 132.55 | 147.48 | 125.04 | 157.71 | 60.30 |
| | | | 3.36 | 2.82 | 681, 714 | 1022 | 1607 | 1675 | | | | | |
| *IV* | 13.30 | 3.80 | 219.3 | 295.5 | 661, 709 | 1016 | 1607 | 1657 | 131.70 | 147.90 | 124.49 | 158.40 | 61.57 |
| | | | 3.95 | 2.63 | 652, 726 | 1022 | 1607 | 1679 | | | | | |
| *V* | 9.60 | 2.17 | 219.5 | 287.0 | 655, 707 | 1035 | 1616 | 1653 | 139.30 | 144.83 | 133.97 | 159.31 | 72.35 |
| | | | 3.32 | 2.88 | 654, 723 | 1039 | 1621 | 1667 | | | | | |
| *VI* | 10.44 | 4.23 | 210.0 | 330.0 | 654, 732 | 1018 | 1624 | 1659 | 134.88 | 144.95 | 138.39 | 158.92 | 62.97 |
| | | | 3.22 | 2.92 | 652, 722 | 1021 | 1629 | 1669 | | | | | |
| *VII* | 12.76 | 4.11 | 213.0 | 298.0 | 651, 711 | 1020 | 1605 | 1658 | 131.50 | 147.60 | 124.40 | 158.01 | 61.39 |
| | | | 3.38 | 2.68 | 652, 712 | 1023 | 1606 | 1674 | | | | | |
| *VIII* | 9.30 | 4.32 | 212.5 | 288.0 | 656, 695 | 1012 | 1615 | 1640 | 134.20 | 145.08 | 138.19 | 158.79 | 63.15 |
| | | | 3.40 | 2.73 | 689, 720 | 1011 | 1615 | 1653 | | | | | |
| *IX* | 9.73 | 1.54 | 212.5 | 286.5 | 659, 718 | 1045 | 1624 | 1648 | 133.70 | 144.70 | 138.38 | 158.90 | 64.90 |
| | | | 3.25 | 2.67 | 656, 732 | 1040 | 1622 | 1661 | | | | | |
| *X* | 10.70 | 5.77 | 212.5 | 287.5 | 656, 714 | 1023 | 1623 | 1646 | 133.70 | 148.62 | 138.71 | 158.10 | 63.15 |
| | | | 3.32 | 2.70 | 659, 731 | 1026 | 1625 | 1662 | | | | | |
| *XI* | 10.53 | 2.45 | 213.3 | 296.5 | 655, 684 | 1017 | 1615 | 1653 | 134.85 | 145.47 | 137.93 | 158.72 | 62.91 |
| | | | 3.24 | 2.78 | 685, 721 | 1030 | 1622 | 1664 | | | | | |
| *XII* | 12.56 | 2.85 | 213.0 | 284.0 | 658, 707 | 1031 | 1615 | 1639 | 134.20 | 144.90 | 139.13 | 159.40 | 69.80 |
| | | | 3.37 | 2.69 | 657, 720 | 1034 | 1615 | 1653 | | | | | |
| *XIII* | 9.96 | 4.23 | 213.0 | 285.5 | 657, 702 | 1003 | 1615 | 1637 | 133.80 | 144.80 | 138.40 | 159.05 | 63.15 |
| | | | 3.30 | 2.67 | 653, 718 | 995 | 1611 | 1650 | | | | | |

*Table 2* (Continued)

| Compound | $\mu$ / $10^{-30}$ C m | log *x* | $\lambda_{max}$/nm log($\varepsilon$/(m$^2$ mol$^{-1}$)) | | $\tilde{\nu}$/cm$^{-1}$ (CHCl$_3$/CCl$_4$) ν(P=S) | ν(P—O—C$_{aliph}$) | ν(C=N) | ν(C=O) | δ/ppm $^{13}$C-6 | $^{13}$C-5 | $^{13}$C-4 | $^{13}$C-3 | $^{31}$P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *XIV* | 10.63 | 3.40 | 212.3 | 285.7 | 655, 704 | 996 | 1615 | 1641 | 133.90 | 144.88 | 138.50 | 159.18 | 62.48 |
| | | | 3.30 | 2.69 | 655, 722 | 996 | 1614 | 1653 | | | | | |
| *XV* | 10.26 | 2.48 | 214.0 | 285.5 | 659, 733 | 1037 | 1620 | 1644 | 133.80 | 144.79 | 138.40 | 158.90 | 63.16 |
| | | | 3.25 | 2.67 | 659, 729 | 1038 | 1622 | 1660 | | | | | |
| *XVI* | 11.23 | 4.25 | 209.0 | 325.0 | 655, 712 | 1021 | 1589 | 1661 | 132.67 | 148.14 | 128.45 | 159.70 | 62.05 |
| | | | 3.29 | 2.94 | 663, 722 | 1029 | 1587 | 1670 | | | | | |
| *XVII* | 10.90 | 2.81 | 213.0 | 285.0 | 655, 721 | 1036 | 1619 | 1647 | 134.20 | 144.69 | 139.17 | 159.30 | 69.99 |
| | | | 3.29 | 2.65 | 658, 719 | 1037 | 1624 | 1662 | | | | | |
| *XVIII* | 11.40 | 3.93 | 211.5 | 285.5 | 657, 685 | 1014 | 1625 | 1645 | 133.90 | 144.80 | 138.60 | 159.10 | 63.58 |
| | | | 3.28 | 2.67 | 657, 721 | 1019 | 1624 | 1663 | | | | | |
| *XIX* | 10.40 | 2.74 | 213.0 | 286.0 | 656, 695 | 1006 | 1623 | 1645 | 133.80 | 144.80 | 138.40 | 159.07 | 61.88 |
| | | | 3.25 | 2.67 | 658, 720 | 1005 | 1624 | 1664 | | | | | |
| *XX* | 10.06 | 3.43 | 212.5 | 285.0 | 654, 703 | 1015 | 1608 | 1634 | 133.80 | 144.80 | 138.40 | 159.05 | 63.39 |
| | | | 3.29 | 2.67 | 653, 723 | 1022 | 1617 | 1655 | | | | | |
| *XXI* | 9.83 | 5.68 | 213.0 | 289.0 | 653, 699 | 1018 | 1617 | 1641 | 133.30 | 144.30 | 138.00 | 158.79 | 63.15 |
| | | | 3.32 | 2.72 | 657, 703 | 1021 | 1625 | 1654 | | | | | |
| *XXII* | 12.83 | 4.53 | 213.0 | 287.5 | 655, 724 | 1021 | 1621 | 1647 | 133.58 | 144.50 | 137.83 | 158.59 | 63.39 |
| | | | 3.32 | 2.69 | 654, 720 | 1019 | 1624 | 1659 | | | | | |
| *XXIII* | 12.33 | 4.56 | 212.5 | 296.5 | 654, 693 | 1019 | 1604 | 1667 | 131.89 | 147.80 | 124.70 | 158.01 | 61.21 |
| | | | 3.43 | 2.71 | 667, 720 | 1025 | 1606 | 1670 | | | | | |
| *XXIV* | 14.10 | 5.02 | 211.0 | 299.0 | 653, 705 | 1020 | 1608 | 1674 | 133.40 | 147.80 | 125.30 | 157.80 | 61.15 |
| | | | 3.33 | 2.80 | 673, 715 | 1019 | 1613 | 1689 | | | | | |
| *XXV* | 12.50 | 4.10 | 212.0 | 295.0 | 655, 721 | 1018 | 1605 | 1657 | 132.19 | 147.80 | 124.50 | 157.70 | 61.27 |
| | | | 3.32 | 2.67 | 656, 729 | 1022 | 1604 | 1677 | | | | | |
| *XXVI* | 9.76 | 3.34 | 214.3 | 280.0 | 662, 679 | 1022 | 1622 | 1652 | 133.80 | 144.80 | 138.30 | 159.11 | 63.39 |
| | | | 3.37 | 2.71 | 658, 672 | 1027 | 1622 | 1662 | | | | | |
| *XXVII* | 9.36 | 3.33 | 212.0 | 286.0 | 655, 706 | 1019 | 1612 | 1640 | 133.70 | 144.95 | 138.40 | 159.05 | 58.30 |
| | | | 3.36 | 2.67 | 652, 720 | 1020 | 1618 | 1657 | | | | | |

*Table 2* (Continued)

| Compound | $\mu$ / $10^{-30}$ C m | log $x$ | $\lambda_{max}$/nm, log ($\varepsilon$/($m^2$ $mol^{-1}$)) | | $\tilde{\nu}$/$cm^{-1}$ ($CHCl_3$/$CCl_4$) | | | | $\delta$/ppm | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ν(P=S) | ν(P—O—$C_{aliph}$) | ν(C=N) | ν(C=O) | $^{13}$C-6 | $^{13}$C-5 | $^{13}$C-4 | $^{13}$C-3 | $^{31}$P |
| *XXVIII* | 10.33 | 2.77 | 212.5 | 285.5 | 654, 704 | 1006 | 1613 | 1636 | 133.90 | 144.88 | 138.40 | 159.10 | 63.33 |
| | | | 3.30 | 2.67 | 652, 720 | 1005 | 1616 | 1652 | | | | | |
| *XXIX* | 11.96 | 4.45 | 210.5 | 324.0 | 654, 702 | 1006 | 1570 | 1635 | 131.76 | 149.40 | 127.73 | 160.35 | 61.50 |
| | | | 3.19 | 2.84 | 670, 723 | 1017 | 1576 | 1642 | | | | | |
| *XXX* | 10.26 | 2.82 | 212.5 | 286.0 | 657, 676 | 1026 | 1626 | 1652 | 133.90 | 144.88 | 138.50 | 159.10 | 63.64 |
| | | | 3.29 | 2.69 | 655, 722 | 1023 | 1622 | 1658 | | | | | |
| *XXXI* | 9.96 | 3.73 | 212.5 | 286.0 | 654, 713 | 1015 | 1624 | 1646 | 133.77 | 144.80 | 138.30 | 158.98 | 63.09 |
| | | | 3.30 | 2.69 | 653, 725 | 1013 | 1618 | 1658 | | | | | |
| *XXXII* | 10.13 | 4.01 | 212.5 | 286.0 | 662, 709 | 1007 | 1623 | 1644 | 133.77 | 144.70 | 138.50 | 158.90 | 62.40 |
| | | | 3.29 | 2.65 | 663, 707 | 1006 | 1621 | 1662 | | | | | |
| *XXXIII* | 10.96 | 5.84 | 214.0 | 307.0 | 665, 723 | 1025 | 1608 | 1653 | 131.20 | 147.20 | 124.10 | 158.01 | 61.21 |
| | | | 3.34 | 2.72 | 665, 731 | 1019 | 1607 | 1666 | | | | | |
| *XXXIV* | 10.73 | 4.29 | 211.0 | 322.0 | 658, 714 | 1018 | 1582 | 1644 | 131.75 | 149.21 | 127.83 | 159.89 | 61.82 |
| | | | 3.21 | 2.85 | 670, 721 | 1032 | 1583 | 1651 | | | | | |
| *XXXV* | 11.66 | 2.48 | 212.5 | 296.0 | 654, 673 | 1026 | 1608 | 1662 | 131.72 | 147.91 | 124.36 | 158.27 | 61.21 |
| | | | 3.36 | 2.65 | 647, 726 | 1030 | 1610 | 1679 | | | | | |
| *XXXVI* | 12.40 | 4.68 | 219.0 | 297.0 | 663, 713 | 1026 | 1606 | 1660 | 131.60 | 147.70 | 124.52 | 158.07 | 61.34 |
| | | | 3.05 | 2.68 | 660, 730 | 1020 | 1606 | 1666 | | | | | |
| *XXXVII* | 11.23 | 4.28 | 211.5 | 321.0 | 660, 694 | 1034 | 1584 | 1649 | 131.91 | 149.14 | 127.90 | 159.96 | 61.70 |
| | | | 3.31 | 2.84 | 670, 722 | 1033 | 1581 | 1652 | | | | | |

$x$ — partition coefficient; eluant: 60 vol. % MeOH and 40 vol. % $H_2O$.

*Table 3*

Insecticidal, acaricidal, and fungicidal activity of compounds prepared

| Compound | Contact activity $(LC_{50})/(mg\,dm^{-3})$[a] | | $(ED_{50})/(mg\,dm^{-3})$[b] |
|---|---|---|---|
| | *Aphis fabae* | *Tetranychus urticae* | *Erysiphe graminis* |
| *I* | 100.0 | 500.0 | 791.5 |
| *II* | 63.6 | 2000.0 | 42.3 |
| *III* | 1933.0 | 850.0 | 8962.0 |
| *IV* | 25.4 | 900.0 | 3000.0 |
| *V* | 733.0 | 650.0 | 300.0 |
| *VI* | 1466.0 | 5000.0 | 1888.0 |
| *VII* | 500.0 | 480.0 | 4219.0 |
| *VIII* | 220.0 | 1000.0 | 1685.0 |
| *IX* | 633.0 | 6.9 | 12.1 |
| *X* | 19.0 | 5200.0 | 614.0 |
| *XI* | 59.7 | 500.0 | 1010.0 |
| *XII* | 8.3 | 1100.0 | 2473.0 |
| *XIII* | 5.4 | 2500.0 | 18.8 |
| *XIV* | 4.5 | 980.0 | 78.5 |
| *XV* | 2.1 | 2.3 | 9.9 |
| *XVI* | 2333.0 | 500.0 | 4641.0 |
| *XVII* | 10.0 | 1050.0 | 3000.0 |
| *XVIII* | 11.0 | 500.0 | 31.5 |
| *XIX* | 1.9 | 5.2 | 16.6 |
| *XX* | 126.6 | 500.0 | 14.1 |
| *XXI* | 380.0 | 2000.0 | 118.6 |
| *XXII* | 60.1 | 2500.0 | 77.4 |
| *XXIII* | 1666.0 | 980.0 | 38047.0 |
| *XXIV* | 2333.0 | 900.0 | 9819.0 |
| *XXV* | 2000.0 | 900.0 | 6000.0 |
| *XXVI* | 2.1 | 1050.0 | 7.6 |
| *XXVII* | 1.9 | 3500.0 | 1222.0 |
| *XXVIII* | 9.5 | 28.0 | 1.9 |
| *XXIX* | 500.0 | 750.0 | 303.0 |
| *XXX* | 8.3 | 53.0 | 41.2 |
| *XXXI* | 300.0 | 250.0 | 37.2 |
| *XXXII* | 450.0 | 1300.0 | 36.2 |
| *XXXIII* | 2333.0 | 1000.0 | 6000.0 |
| *XXXIV* | 406.2 | 4500.0 | 2000.0 |
| *XXXV* | 566.0 | 350.0 | 2000.0 |
| *XXXVI* | 500.0 | 1700.0 | 2000.0 |
| *XXXVII* | 800.0 | 650.0 | 6000.0 |

*Table 3* (Continued)

| Compound | Contact activity $(LC_{50})/(mg\,dm^{-3})^a$ | | $(ED_{50})/(mg\,dm^{-3})^b$ |
|---|---|---|---|
| | *Aphis fabae* | *Tetranychus urticae* | *Erysiphe graminis* |
| Fenitrothion | 3.8 | — | — |
| Carbophenothion | — | 0.75 | — |
| Ethirimol | — | — | 82.6 |
| Triadimefon | — | — | 5.6 |

*a*) $LC_{50}$ — concentration required to kill 50 % of the test species.
*b*) $ED_{50}$ — dose required to kill 50 % of the test species.

was registered with a number of compounds having the substituents $R^1 = ClCH_2CH_2$, $R^3 = CH_3O$, $R^4 = CH_3$, and $R^2$ = alkoxy; among them compounds *XIV*, *XV*, *XXVI*, and *XXVII* showed a higher activity than the standard fenitrothion. Compounds *XII*—*XIV*, *XXVIII*, and *XXX* were practically on the level of the standard. The high activity of compound *XXVII* having $R^2$ = phenoxy is interesting. In tests for the acaricidal activity none of the compounds reached the activity of the used standard carbophenothion, but compounds *IX*, *XV*, and *XIX* showed a very good activity. In tests for ovicidal activity none of the compounds reached a significant activity at the concentrations used.

It was found that by testing for fungicidal activity compounds prepared were, excepting antipowdery mildew activity, inactive on other test objects at the concentration used. A remarkable fungicidal activity against *Erysiphe graminis* was observed with *O*-(2-chloroethyl)-*O*-alkoxy-*O*-(2-methyl-4-methoxy-3-oxo--2*H*-pyridazine-5-yl)thiophosphates, from which n-propyl derivative (compound *XXVIII*) was more active than the standard triadimephon. Compounds *XXVI* (*O*-isobutyl) and *XV* (*O*-ethyl) were as active as the standard used. Highly active were also compounds *IX* (*O*-methyl), *XIX* (*O*-isopropyl), and *XIII* (*O*--isopentyl) which were only sligthly less active than the standard used. Compounds *II*, *XIV*, *XVIII*, *XXII*, *XXX*, *XXXI*, and *XXXII* were more active than the used standard ethirimol.

## Experimental

Infrared spectra of compounds prepared were recorded with a UR 20 (Zeiss, Jena) instrument in tetrachloromethane or trichloromethane ($c = 0.10$—$0.15\,mol\,dm^{-3}$, cell thickness 0.113 mm). The wavenumber calibration was checked against the spectrum of polystyrene. Ultraviolet spectra were recorded with a Specord UV VIS (Zeiss, Jena) instrument in methanol ($c = 2\times10^{-5}$—$5\times10^{-5}\,mol\,dm^{-3}$, cell thickness 10 mm). $^{13}C$ NMR spectra were recorded with an FX-60 Jeol instrument (15.03 MHz) in $C^2HCl_3$ using TMS as internal standard. $^{31}P$ NMR spectra were recorded with an FX-100 Jeol instrument (40.26 MHz) in $C^2HCl_3$ using $H_3PO_4$ (85 %) as external standard. Assignment of the signals and interaction constants was made by a comparison of those of compounds with similar structures in the literature [9—11].

The dipole moments of the compounds were calculated from the Halverstadt—Cumler relation. The corresponding dielectric constants of the compounds were measured on a DM 01 instrument in benzene solution at 25 °C. The densities of compounds prepared were measured by a pycnometer at 25 °C [12].

The partition coefficients of compounds studied were measured on HPLC Varian 8500 with a column MicroPac C-18, 25 cm long, diameter 2.7 mm at 25 °C and the flow rate 40 $cm^3 h^{-1}$. A solution of water—methanol was used as the mobile phase, a buffer sodium dihydrogen phosphate ($c = 0.01$ mol $dm^{-3}$) was used for maintaining the pH of solutions [13—15].

Purity of compounds was verified by means of thin-layer chromatography on Silufol R with a luminescent indicator UV 254 (Lachema, Brno), a mixture of benzene—propanone (volume ratio = 9 : 1, resp. 8 : 2) was applied as a developing agent. Detection was carried out by means of 0.5 % solution of 2,6-dibromoquinone-4-chloroimide in petroleum ether at 120 °C, under UV light ($\lambda = 254$ nm). Column chromatography was carried out on a silica gel column (L 93—149 μm, Lachema, Brno). Before use, the silica gel was activated for 4 h at 140 °C. Toluene with an addition of propanone ($\varphi = 0$—10 vol. %) was used as eluant. The separation of the compounds was monitored by means of TLC.

The compounds prepared were tested for contact insecticidal activity using testing objects as *Musca domestica* L., *Sitophylus granarius*, and *Aphis fabae*; for systemic insecticidal activity using *Aphis fabae*. The acaricidal and ovicidal activity was followed on females and eggs of *Tetranychus urticae* KOCH.

Fungicidal activity of prepared compounds was followed by both the *in vitro* and *in vivo* methods. The proper inherent activity was followed by the glass slide method on spores of fungi *Aspergillus niger* V. TIEGH. and *Cladosporium cucumerinum* ELL. et ARTH. after the Sharvell method. Antipowdery mildew activity was followed on *Erysiphe graminis* (on the living plants of spring barley, sort Dunajský trh) and on *Phytophtora infestans* (MONT.) de BARY (on tomatoes) [16]. The mordant activity was followed on dead caryopsis of rye infected by conidia of fungi *Fusarium nivale* (SR.) CES. [17]. Pesticidal activity of compounds prepared was followed after previously described methods [6].

### *Procedure A*

## Compounds *I—VI, VIII—XXI, XXIV—XXXVII*

To solution or suspension of the potassium or sodium salt of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol in butanone and in acetonitrile, respectively, or to a solution of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol (0.11 mol) and potassium or sodium carbonate (0.11 mol) *O*-(haloalkyl)-*O*-(alkyl, aryl)-(*N*-alkylamido, *N*,*N*-dialkylamido)-chlorothiophosphate (0.1 mol) was added at 20 °C. After addition the mixture was stirred for 3—6 h under reflux. After cooling toluene (100 $cm^3$) was added and the mixture was washed with water and with an aqueous solution of sodium hydrogen carbonate (5 % solution). After separation, the toluene layer was dried with anhydrous sodium sulfate and toluene was removed under reduced pressure. A distilled residue was purified by the column chromatography on silica gel using a mixture of toluene and propanone as eluant ($\varphi$ = 0—10 vol. %).

*Procedure B*

Compounds *IV—VII*, *XXII—XXVI*, *XXXIII*, and *XXXVI*

To a mixture of 2,4-disubstituted 3-oxo-2*H*-pyridazine-5-ol (0.025 mol), potassium carbonate or sodium carbonate (0.025 mol) and quaternary ammonium salt (0.0013 mol) in water (10—20 $cm^3$) the appropriate *O*-(haloalkyl)-*O*-(alkyl, aryl)-(*N*-alkylamido, *N*,*N*-dialkylamido)chlorothiophosphate (0.025 mol) in toluene (100 $cm^3$) was gradually added with vigorous stirring at 20 °C. After addition the mixture was stirred for 2 h at 20 °C. The presence of starting compounds was indicated by TLC, the mixture was heated to 40—60 °C for about 1—2 h. After cooling the reaction mixture was treated as by procedure *A*.

## References


1. Mineicki, O., *Jpn. Pestic. Inf. 1977*, No. 33, 9.
2. Konečný, V., *Pestic. Sci. 4*, 775 (1973).
3. Konečný, V., Varkonda, Š., and Vargová, M., *Pestic. Sci. 7*, 107 (1976).
4. Konečný, V. and Kováč, Š., *Pestic. Sci. 9*, 571 (1978).
5. Konečný, V., Kováč, Š., Varkonda, Š., and Šustek, J., *Pestic. Sci. 10*, 227 (1979).
6. Konečný, V., Varkonda, Š., Kovačičová, J., Bátora, V., and Vargová, M., *Pestic. Sci. 10*, 139 (1979).
7. Konečný, V., *Pestic. Sci. 7*, 97 (1976).
8. Žúžiová, J. and Konečný, V., *Czechoslov.* 235190 (1984).
9. Emsley, J. and Hall, D., *Phosphorus Chemistry*. Harper and Row, London, 1976.
10. Mavel, G., in *Annual Reports on NMR Spectroscopy*, Vol. *58*. P. 261. Academic Press, New York, 1973.
11. Pragosin, P. S. and Kunz, R. W., *$^{31}$P and $^{13}$C NMR of Transition Complexes*. Springer-Verlag, Berlin, 1979.
12. Vogel, A. I., Cresswell, W. T., Jeffery, G. H., and Laicester, J., *J. Chem. Soc. 1952*, 514.
13. Carlson, R. M., Carlson, R. E., and Koppermen, H. L., *J. Chromatogr. 107*, 219 (1975).
14. McCall, J. M., *J. Med. Chem. 18*, 549 (1975).
15. Mirrlees, M. S., Moulton, S. J., Murphy, C. T., and Taylor, P. J., *J. Med. Chem. 19*, 615 (1976).
16. Demečko, J. and Konečný, V., *Agrochémia* (Bratislava) *10*, 127 (1970).
17. Konečný, V., Demečko, J., and Sutoris, V., *Acta Fac. Rerum Nat. Univ. Comenianae (Chimia) 20*, 39 (1974).


Translated by Š. Kováč