Phosphorylated isothioureas
V. Preparation and properties of 3-phosphorylated and 3-thiophosphorylated 1,1,2-trisubstituted isothioureas

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The synthesis and properties of 3-[(R^1, R^2)-phosphoryl- and -thiophosphoryl]-1,1-(R^3, R^4)-2-(R^5)isothioureas are described. They were prepared by alkylation of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkyl- and -1,1-(3′-oxapentamethylene)thioureas with alkyl halides, aralkyl halides, and dimethyl sulfate in organic solvent in the presence of agents binding hydrogen halide or with diazomethane in ether, further by the reaction of dialkyl amidothiophosphates with mercaptoformamide chlorides in benzene in the presence of triethylamine, or by the reaction of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkyl-2-alkylisothioureas with alkyl halides in the presence or absence of a solvent, by the reaction of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkylthioureas with alkyl halides, by the reaction of *O*,*O*-dialkyl chlorothiophosphate with the appropriate thiouronium salts, and by the reaction of N^1,N^1-diethyl-N^2-(dichlorophosphoryl)chloroformamidine with butanethiol and methanol in acetonitrile in the presence of triethylamine. The i.r., u.v., and ^{1}H-n.m.r. spectra of the synthesized compounds are interpreted and the results of tests for pesticidal activity are discussed.

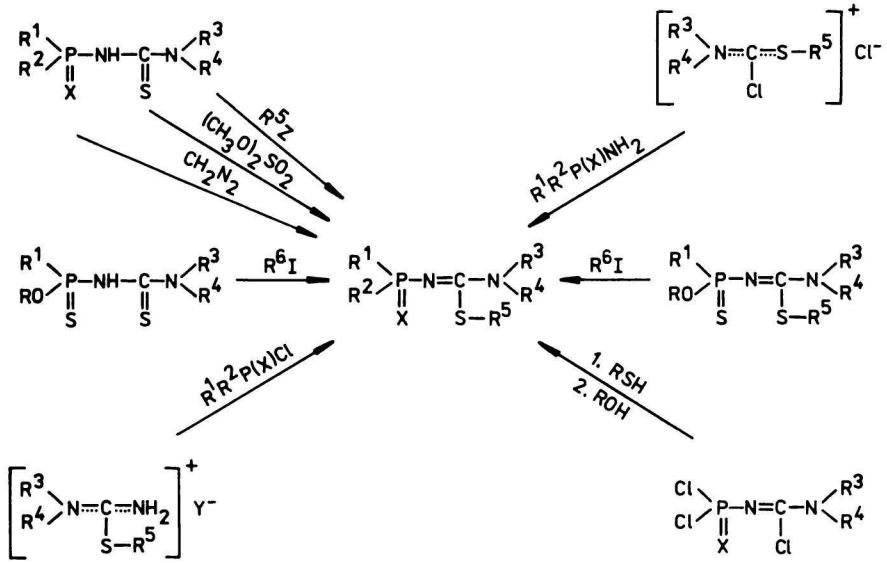
Описывается синтез и свойства 3-[(R^1, R^2)-фосфорил- и тиофосфорил]-1,1-(R^3, R^4)-2-(R^5)изотиомочевин, приготовленных алкилированием 3-(*O*,*O*-диалкилтиофосфорил)-1,1-диалкил- и -1,1-(3′-оксапентаметилен)тиомочевин алкилгалогенидами, аралкилгалогенидами и диметилсульфатом в органических растворителях в присутствии реагентов, связывающих галогенводород, или диазометаном в эфире, дальше при помощи реакции диалкиламидотиофосфатов с хлоридами меркаптоформамида в бензоле в присутствии триэтиламина, или по реакции 3-(*O*,*O*-диалкилтиофосфорил)-1,1-диалкил-2-алкилизотиомочевин с алкилгалогенидами в присутствии или в отсутствии растворителя, по реакции 3-(*O*,*O*-диалкилтиофосфорил)-1,1-диалкилтиомочевин с алкилгалогенидами, по реакции *O*,*O*-диалкилхлортиофосфата с соответственными солями тиоуро-

ния, и по реакции N^1,N^1-диэтил-N^2-(дихлорфосфорил)хлорформамидина с бутантиолом и метанолом в ацетонитриле в присутствии триэтиламина. Приводятся и обсуждаются ИК, УФ и ^{1}H-ЯМР спектры и пестицидное действие синтезированных соединений.

In our previous works synthesis, properties, and structures of 3-(*O*,*O*-dialkylthiophosphoryl)-2-alkyl(aralkyl) substituted isothioureas [1], 3-(*O*,*O*-dialkyl- and diphenylphosphoryl)-2-alkyl(aralkyl) substituted isothioureas [2], 3-(*O*-alkyl--*N*-alkylamidothiophosphoryl)-, 3-(*O*-methyl-*N*,*N*-dimethylamidothiophosphoryl)-, 3-(*O*-alkyl-*S*-alkylthiophosphoryl)-, and 3-(*O*-alkyl-*P*-alkylthiophosphonyl)-2-alkyl substituted isothioureas [3], and 3-(dialkyl(thio)phosphoryl)-1--alkyl(aryl)-2-alkyl(aralkyl)isothioureas [4] were described.

The preparation of 3-(*O*,*O*-diethylphosphoryl)-1,1-dimethyl-2-butyl- and -2-propylisothioureas by the reaction of *N*-[*O*,*O*-diethyl(chloro)phosphoryl]dichloromethylenimine with butanethiol and propanethiol, respectively, in 60 and 44% yields, is known from the literature [5]. The reported method is, however, too complicated and gives relatively low yields. Therefore, the aim of the present work was to search for more suitable methods for the preparation of the studied compounds and investigate their physicochemical and pesticidal properties.

The methods chosen for the synthesis are illustrated in Scheme 1



Scheme 1

Experimental

O-Methyl *O*-isopropyl chlorothiophosphate [6] was prepared after the known method from phosphorus(V) sulfide chloride and isopropyl alcohol and by treatment of the formed *O*-isopropyl dichlorothiophosphate with sodium methoxide. *O*,*O*-Dimethyl amidothiophosphate [7, 8] was prepared by the reaction of phosphorus(V) sulfide chloride with methanol and by treatment of the formed *O*,*O*-dimethyl chlorothiophosphate with gaseous ammonia [9]. *O*,*S*-Dimethyl amidothiophosphate [10] was prepared by treatment of *O*,*O*-dimethyl amidothiophosphate with dimethyl sulfate [7, 8]. 3-(*O*,*O*-Diethylthiophosphoryl)-1,1-dimethylthiourea [11], 1,1-(3′-oxapentamethylene)thiourea [11], and 1,1-diallylthiourea [14] were prepared by the reaction of *O*,*O*-diethylthiophosphoryl isothiocyanate [12, 13] with gaseous dimethylamine, morpholine, and diallylamine, respectively. 3-(*O*-Ethyl-*O*-isopropylthiophosphoryl)-1,1-dimethylthiourea [14] and 1,1-dipropylthiourea, respectively [14] were prepared by the reaction of *O*-ethyl-*O*-isopropylthiophosphoryl isothiocyanate [14] with gaseous dimethylamine and dipropylamine, respectively. *N*,*N*-Dimethyl(methylthio)formamide chloride and *N*,*N*-dimethyl(phenylthio)formamide chloride [15, 16] were prepared by the reaction of *S*-methyl *N*,*N*-dimethyldithiocarbamate [17] and *S*-phenyl *N*,*N*-dimethyldithiocarbamate [18] with phosgene. 1-Methyl-1-phenyl-2-benzylthiouronium chloride [14] was prepared by treatment of 1-methyl-1-phenylthiourea with benzyl chloride in ethanol under reflux. N^1,N^1-Diethyl-N^2-(dichlorophosphoryl)chloroformamidine [19] was prepared by treatment of diethyl cyanide with phosphorus(V) oxide chloride at 95—100°C during 40 h.

The data of elemental analysis, yields, reaction conditions, eluents, R_f, n_D^{20}, and m.p. values are presented in Table 1.

Infrared spectra of the investigated compounds were measured on UR-20 and IR-71 Zeiss spectrophotometers in CCl_4 and $CHCl_3$. The instruments were calibrated by polystyrene foil; the reading accuracy was ± 1 cm^{-1}. The u.v. spectra were taken with a Unicam SP 8000 spectrophotometer ($d = 1$ cm, $c = 10^{-4}$ to 10^{-5} M in methanol). The ^{1}H-n.m.r. spectra were measured on a Tesla BS 487C apparatus at 80 MHz in $CDCl_3$ (99.5% D-isotope) at 25°C using TMS as internal standard.

Thin-layer chromatography (t.l.c.) on Silufol R UV 254 (Kavalier, Votice) with luminescent indicator and on Silufol R (Kavalier, Votice) without indicator was used to follow the purity of compounds and the reaction course as well as to determine the R_f values. The compounds were detected with u.v. light ($\lambda = 254$ nm) and by spraying the plates with 0.5% petroleum ether solution of DCQ (2,6-dibromo-4-chloroimidoquinone) and heating at 120°C for 2—5 min.

The contaminated liquid compounds were purified by column chromatography on Silica gel L 100/160 mesh (Lachema, Brno). Mixtures of benzene and acetone, chloroform and acetone, or petroleum ether and acetone were used as eluents; the acetone concentration increased from 0 to 20%.

Some of the liquid compounds were purified also on silica gel plates (Silica gel H Merck for t.l.c.) by elution with some of the eluents listed in Table 1. Part of the layer was detected by DCQ and at the corresponding R_f the silica gel was scraped and the product was eluted with acetone.

Table 1

Characterization of the synthesized compounds

Compound	R^1 R^2	R^3 R^4	R^5	X	Formula *M*	Calculated/found % N	% P	% S	Yield, % Method of preparation	Reaction time, h *T*, °C	n_D^{20} M.p., °C	T.l.c. R_f
I	CH_3O	CH_3	CH_3	S	$C_6H_{15}N_2O_2PS_2$	11.55	12.77	26.40	78.9 *E*	4	1.5716	0.09[b]
	CH_3O	CH_3			242.28	11.86	12.90	26.80		50	*g*	0.17[d]
												0.54[e]
II	CH_3O	CH_3	Ph	S	$C_{11}H_{17}N_2O_2PS_2$	9.20	10.17	21.10	57.2 *E*	5	59—60	0.09[b]
	CH_3O	CH_3			304.34	8.71	10.09	20.81		50		0.09[d]
												0.84[e]
III	CH_3O	C_2H_5	iC_4H_9	O	$C_{11}H_{25}N_2O_3PS$	9.45	10.45	10.82	41.5 *I*	5	1.5257	0.11[a]
	CH_3O	C_2H_5			296.33	9.91	10.87	11.32		23		0.0[b]
												0.09[c]
IV	CH_3O	CH_3	$PhCH_2$	S	$C_{19}H_{25}N_2O_2PS_2$	6.86	7.58	15.70	53.6 *D*	11	1.5939	0.20[b]
	iC_3H_7O	Ph			408.53	6.52	7.91	16.12		45		0.28[d]
												0.28[e]
V	C_2H_5O	CH_3	CH_3	S	$C_8H_{19}N_2O_2PS_2$	10.35	11.34	23.34	74.8 *B*	6	1.5508	0.08[b]
	C_2H_5O	CH_3			270.30	10.62	10.8	23.85	(92.1 *C*)	58	*f*	0.32[d]
												0.59[e]
VI	C_2H_5O	CH_3	C_2H_5	S	$C_9H_{21}N_2O_2PS_2$	9.82	10.85	22.4	87.4 *A*	12	1.5430	0.10[b]
	C_2H_5O	CH_3			284.39	10.1	10.43	22.89		56		0.38[d]
												0.60[e]
VII	C_2H_5O	CH_3	$CH_2=CHCH_2$	S	$C_{10}H_{21}N_2O_2PS_2$	9.46	10.46	21.66	81.2 *A*	8	1.5558	0.14[b]
	C_2H_5O	CH_3			296.41	9.35	9.83	21.2		56		0.36[d]
												0.52[e]
VIII	C_2H_5O	CH_3	C_3H_7	S	$C_{10}H_{23}N_2O_2PS_2$	9.40	10.39	21.52	83.7 *A*	10	1.5378	0.10[b]
	C_2H_5O	CH_3			298.42	9.34	10.20	21.90		56		0.38[d]
												0.62[e]

Table 1 (Continued)

Compound	R^1 R^2	R^3 R^4	R^5	X	Formula *M*	Calculated/found % N	% P	% S	Yield, % Method of preparation	Reaction time, h *T*, °C	n_D^{20} M.p.,°C	T.l.c. R_f
IX	C_2H_5O	CH_3	iC_3H_7	S	$C_{10}H_{23}N_2O_2PS_2$	9.40	10.39	21.52	60.4 *A*	20	1.5301	0.13[b]
	C_2H_5O	CH_3			298.42	9.44	9.94	21.83		56		0.39[d]
												0.63[e]
X	C_2H_5O	CH_3	$PhCH_2$	S	$C_{14}H_{23}N_2O_2PS_2$	8.37	8.94	18.51	66.8 *A*	4	34—37	0.13[b]
	C_2H_5O	CH_3			346.46	8.05	8.40	18.18		56		0.18[d]
												0.91[e]
XI	C_2H_5O	O$<^{CH_2CH_2}_{CH_2CH_2}$	$PhCH_2$	S	$C_{16}H_{25}N_2O_3PS_2$	7.23	7.97	16.5	86.5 *A*	8	1.5909	0.05[b]
	C_2H_5O				388.5	6.9	7.51	16.01		56		0.19[d]
												0.02[e]
XII	C_2H_5O	O$<^{CH_2CH_2}_{CH_2CH_2}$	iC_3H_7	S	$C_{12}H_{25}N_2O_3PS_2$	8.23	8.83	18.83	89.7 *A*	12	1.5333	0.04[b]
	C_2H_5O				340.46	7.89	8.99	18.64		56		0.26[d]
												0.60[e]
XIII	C_2H_5O	$CH_2=CHCH_2$	$PhCH_2$	S	$C_{18}H_{27}N_2O_2PS_2$	7.03	7.63	16.09	68.1 *A*	8	1.5848	0.56[b]
	C_2H_5O	$CH_2=CHCH_2$			398.54	6.82	7.31	15.73		56		0.18[d]
												0.75[e]
XIV	C_2H_5O	CH_3	CH_3	S	$C_9H_{21}N_2O_2PS_2$	9.84	10.87	22.6	94.6 *C*	3	1.5381	0.02[b]
	iC_3H_7O	CH_3			284.39	9.63	11.07	23.1		25		0.25[d]
												0.22[e]
XV	C_2H_5O	CH_3	C_4H_9	S	$C_{12}H_{27}N_2O_2PS_2$	8.58	9.49	19.64	70.6 *A*	7	1.5264	0.21[b]
	iC_3H_7O	CH_3			326.47	8.69	9.73	19.20		78		0.22[d]
XVI	C_2H_5O	CH_3	C_8H_{17}	S	$C_{16}H_{35}N_2O_2PS_2$	7.32	8.10	16.76	62.3 *A*	10	1.5089	0.24[b]
	iC_3H_7O	CH_3			382.58	7.88	8.14	16.66		78		0.23[d]
												0.68[e]
XVII	C_2H_5O	CH_3	4Cl—$PhCH_2$	S	$C_{15}H_{24}ClN_2O_2PS_2$	7.09	7.84	16.24	87.8 *A*	1.5	58—60	0.14[b]
	iC_3H_7O	CH_3			394.94	7.41	7.72	15.86		78		0.20[d]
												0.68[e]

Table 1 (Continued)

Compound	R^1 R^2	R^3 R^4	R^5	X	Formula *M*	Calculated/found % N	% P	% S	Yield, % Method of preparation	Reaction time, h *T*, °C	n_D^{20} M.p., °C	T.l.c. R_t
XVIII	C_2H_5O	CH_3	$C_2H_5SCH_2$	S	$C_{11}H_{25}N_2O_2PS_3$	8.13	8.99	27.92	60.5 *A*	2.5	1.5740	0.18[b]
	iC_3H_7O	CH_3			334.49	8.61	9.21	27.81		78		0.13[d]
												0.06[e]
XIX	C_2H_5O	CH_3	$C_2H_5SCH_2CH_2$	S	$C_{12}H_{27}N_2O_2PS_3$	7.81	8.63	26.83	73.7 *A*	3	1.5440	0.16[b]
	iC_3H_7O	CH_3			358.58	7.50	8.99	27.28		78		0.18[d]
												0.06[e]
XX	C_2H_5O	CH_3	4Cl—$PhSCH_2$—	S	$C_{16}H_{26}ClN_2PS_3$	6.35	7.02	21.81	71.8 *A*	4.5	1.5892	0.15[b]
	iC_3H_7O	CH_3	—CH_2		441.03	6.03	7.38	22.36		78		0.27[d]
												0.26[e]
XXI	C_2H_5O	CH_3	$PhCOCH_2$	S	$C_{16}H_{25}N_2O_3PS_2$	7.22	7.97	16.5	71.1 *A*	8	1.5789	0.14[b]
	iC_3H_7O	CH_3			388.50	7.55	8.31	17.1		65		0.28[d]
												0.21[e]
XXII	C_2H_5O	CH_3	$C_2H_5OCOCH_2$	S	$C_{12}H_{25}N_2O_4PS_2$	7.86	8.69	17.99	52.8 *A*	7	1.5157	0.03[b]
	iC_3H_7O	CH_3			356.44	7.41	8.93	18.56		78		0.15[d]
												0.11[e]
XXIII	C_2H_5O	C_3H_7	CH_3	S	$C_{13}H_{29}N_2O_2PS_2$	8.23	9.11	18.83	91.7 *C*	3	1.5131	0.17[b]
	iC_3H_7O	C_3H_7			340.50	8.51	9.46	18.51		25		0.48[d]
												0.30[e]
XXIV	C_2H_5O	C_3H_7	4Cl—$PhCH_2$	S	$C_{19}H_{32}ClN_2O_2PS_2$	6.21	6.87	14.22	73.9 *A*	8	1.5461	0.22[b]
	iC_3H_7O	C_3H_7			451.04	6.03	7.15	14.73		78		0.48[d]
												0.31[e]
XXV	CH_3O	CH_3	CH_3	O	$C_6H_{15}N_2O_2PS_2$	11.55	12.77	26.4	78.9 *E*	2.5	1.5539	0.17[a]
	CH_3S	CH_3			242.38	11.68	12.91	26.38	(91 *G*)	40		0[b]
												0.04[e]

Table 1 (Continued)

Compound	R^1 R^2	R^3 R^4	R^5	X	Formula *M*	Calculated/found % N	% P	% S	Yield, % Method of preparation	Reaction time h *T*, °C	n_D^{20} M.p.,°C	T.l.c. R_f
XXVI	CH_3O	CH_3	CH_3	O	$C_7H_{17}N_2O_2PS_2$	10.92	12.08	25.0	94.2 *G*	4	1.5607	0.24[a]
	C_2H_5S	CH_3			256.34	10.80	11.92	24.8		72		0[b]
												0.18[c]
XXVII	C_2H_5O	CH_3	CH_3	O	$C_7H_{17}N_2O_2PS_2$	10.92	12.08	25.0	86.7 *F*	14	1.5424	0.29[a]
	CH_3S	CH_3			256.34	10.82	11.81	24.6		40		0[b]
												0.22[c]
XXVIII	C_2H_5O	CH_3	C_2H_5	O	$C_9H_{21}N_2O_2PS_2$	9.84	10.87	22.58	91.6 *F*	26	1.5456	0.39[a]
	C_2H_5S	CH_3			284.39	9.64	10.50	22.91		75		0[b]
												0.54[c]
XXIX	C_2H_5O	CH_3	CH_3	O	$C_9H_{21}N_2O_2PS_2$	9.84	10.87	22.58	93.2 *G*	20	1.5447	0.49[a]
	C_3H_7S	CH_3			284.39	9.75	10.49	23.05		70		0[b]
												0.38[c]
XXX	C_2H_5O	CH_3	C_2H_5	O	$C_{10}H_{23}N_2O_2PS_2$	9.37	10.36	21.45	90.4 *G*	14	1.5415	0.45[a]
	iC_3H_7S	CH_3			298.42	9.61	10.60	21.56		89		0.01[b]
												0.34[c]
XXXI	C_2H_5O	CH_3	iC_3H_7	O	$C_{11}H_{25}N_2O_2PS_2$	8.97	9.91	20.53	71.8 *H*	12	1.5241	0.35[a]
	iC_3H_7S	CH_3			312.44	9.31	9.47	20.98		89		0.02[b]
												0.27[c]
XXXII	C_2H_5O	$CH_2=CHCH_2$	$CH\equiv CCH_2$	O	$C_{15}H_{21}N_2O_2PS_2$	7.82	8.64	17.89	65.4 *H*	6	1.5685	0.59[a]
	$CH\equiv CCH_2S$	$CH_2=CHCH_2$			358.46	7.94	8.39	17.73		84		0.01[b]
												0.67[c]

Mobile phase: *a*) chloroform : ethanol (95 : 5); *b*) benzene; *c*) petroleum ether : acetone (7 : 3); *d*) petroleum ether : acetone (9 : 1); *e*) chloroform.

Compounds *I*, *II*, *V*, *XXV*, *XXVIII* prepared in benzene; *III* in acetonitrile; *IV* in acetonitrile : water (1 : 1); *V*—*XIII* in acetone; *XIV* and *XXIII* in ether; *XV*—*XXII*, *XXIV* in ethanol; *XXVI* in C_2H_5I; *XXVII* in CH_3I; *XXIX* in C_3H_7Br; *XXX* and *XXXI* in iC_3H_7I; *XXXII* in $CH\equiv CCH_2Br$. *f*) B.p. = 146—148°C/26 Pa; *g*) b.p. = 133°C/13 Pa.

Pesticidal activity was followed under the conditions reported in our previous work [1] after the methods published in [20, 21].

Preparation of 3-dialkylthiophosphoryl- and 3-dialkylphosphoryl-1,1-dialkyl- and -1,1-(3'-oxapentamethylene)-2-alkyl-, -2-aralkyl-, and -2-arylisothioureas

Method A

TO 3-(*O*-*O*dialkylthiophosphoryl)-1,1-dialkyl- and -1,1-(3'-oxapentamethylene)thiourea (0.1 mol) and potassium carbonate (0.1 mol) in ethanol (acetone, acetonitrile) (100 ml), alkyl (aralkyl) halide (0.11 mol) was added under stirring and the reaction mixture was heated to reflux. After the reaction was over, the solid compound was filtered off and the filtrate was evaporated under reduced pressure. Benzene (chloroform) (100 ml) was added to the residue. After washing with water and drying, the solvent was distilled off under reduced pressure and the products were purified by column chromatography.

Method B

To 3-(*O*,*O*-diethylthiophosphoryl)-1,1-dimethylthiourea (0.1 mol) and potassium carbonate (0.1 mol) in acetone (200 ml) dimethyl sulfate (0.11 mol) was added under stirring and the reaction mixture was heated to reflux. After the reaction was over, the solid compound was filtrated off and the filtrate was evaporated under reduced pressure. Benzene (100 ml) was added to the residue. After washing with water and drying, the product was purified by redistillation under reduced pressure. The b.p., R_f, and n_D^{20} values as well as the i.r. spectra of the obtained viscous liquid were identical with those of the compound *V* prepared after the method C.

Method C

To 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkylthiourea (0.1 mol) dissolved in ether (100 ml), ether solution of diazomethane (0.12 mol) was added under stirring at laboratory temperature. After 2 h stirring at laboratory temperature ether was distilled off and light viscous liquids were obtained.

Method D

To the reaction mixture consisting of *O*-methyl *O*-isopropyl chlorothiophosphate (0.1 mol), 1-methyl-1-phenyl-2-benzylthiouronium chloride (0.1 mol), potassium carbonate (0.2 mol), and acetonitrile (50 ml) water (50 ml) was added under stirring while the

temperature increased by 5°C. Stirring was continued under the conditions presented in Table 1 and the course of the reaction was followed by t.l.c. After the reaction was over, chloroform (2 × 50 ml) was added to the reaction mixture. Then the chloroform layer was dried, the solvent was distilled off under reduced pressure and the obtained liquid compound was purified by column chromatography.

Method E

To the appropriate mercaptoformamide chloride (0.1 mol) in dry benzene (150 ml) the appropriate amidothiophosphate (0.1 mol) and triethylamine (0.2 mol) were added simultaneously under stirring within 30 min. Stirring was continued at 50°C. After cooling, the reaction mixture was washed with water and dried. Benzene was distilled off under reduced pressure and the compound *I* was purified by redistillation under reduced pressure, the others by column chromatography.

Method F

The reaction mixture consisting of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkyl-2-alkylisothiourea (0.02 mol), alkyl iodide (0.04 mol), and toluene (benzene) (100 ml) was heated to reflux under stirring. After the reaction was over, the volatile portions were distilled off under reduced pressure and the products were purified by column chromatography.

Method G

The reaction mixture consisting of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkyl-2-alkylisothiourea (0.02 mol) and alkyl iodide (0.2 mol) was heated to reflux under stirring. After the reaction was over, the volatile compounds were distilled off under reduced pressure and the products were purified by column chromatography.

Method H

The reaction mixture consisting of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkylthiourea (0.05 mol) and alkyl halide (0.5 mol) was stirred and heated to reflux. After the reaction was over, the volatile compounds were distilled off and the products were purified by column chromatography.

Method I

To N^1,N^1-diethyl-N^2-(dichlorophosphoryl)chloroformamidine (0.05 mol) dissolved in acetonitrile (100 ml) the mixture of 2-methylpropanethiol (0.05 mol) and triethylamine

(0.05 mol) was added under stirring at 0°C within 30 min. Then the reaction mixture was stirred at laboratory temperature for 3 h and after filtration of triethylammonium chloride acetonitrile was distilled off under reduced pressure. Methanol (50 ml) and triethylamine (10.1 g; 0.1 mol) were added to the distillation residue under stirring. After 2 h stirring at laboratory temperature, the formed triethylammonium chloride was removed by filtration and the volatile portions were distilled off under reduced pressure. The obtained product was purified by column chromatography.

Results and discussion

In the previous works [1—4] the most suitable and the most often used method for the preparation of phosphorylated isothioureas was the reaction of thiouronium salts with dialkyl chlorophosphates and dialkyl chlorothiophosphates. In the case of 1,1-dialkyl-2-alkylthiouronium salts the reaction with chlorothiophosphate proceeded on the imino group which reacted much slower than the amino group at the preparation of compounds in the previous works. It was indicated by longer reaction time, higher temperature, lower yield, and higher contamination of products.

The most suitable method for the preparation of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-disubstituted 2-alkyl- and 2-aralkylisothioureas was shown to be the alkylation of 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-disubstituted thioureas with alkylation agents, mainly alkyl halides. Alkyl bromides and alkyl chlorides are more suitable than alkyl iodides because the latter react also on the second possible reaction centre, *i.e.* on phosphorus. Of the examined solvents (acetone, methyl ethyl ketone, acetonitrile, ethanol) ethanol appeared to be most suitable and of the agents binding hydrogen halide (alkali carbonates, alkali hydrogen carbonates, pyridine, triethylamine, *N*,*N*-dimethylaniline) potassium carbonate was proved to be most suitable regarding the yields and the purity of products. The course of alkylations could be well followed by t.l.c. as the starting phosphorylthioureas, as more polar compounds, had lower R_f values than the corresponding phosphorylisothioureas. It was necessary to purify the liquid compounds by column chromatography.

2-Methylisothioureas can be advantageously prepared with diazomethane (the obtained compounds are pure and chromatographic purification is not necessary) or with dimethyl sulfate (chromatographic purification is necessary because the products are contaminated).

The reaction of mercaptoformamide chlorides with dialkylamidothiophosphates in benzene in the presence of triethylamine is very sensitive to moisture. Mercaptoformamide chlorides are hydrolyzed with water to thiol carbamates. Large amounts of impurities are formed in the reaction and it is necessary to purify the

products either by redistillation (if they are distillable) or by column chromatography.

When using one equivalent of isobutanethiol and triethylamine and one equivalent of N^1,N^1-diethyl-N^2-(dichlorophosphoryl)chloroformamidine and subsequent excess amount of methanol and other two equivalents of triethylamine, the compound *III* is obtained but in a low yield and very contaminated. When three equivalents of isobutanethiol and triethylamine and three equivalents of sodium isobutyl sulfide, respectively were used, a mixture of several compounds was obtained.

The preparation of isomeric 3-(*O*,*S*-dialkylthiophosphoryl)-1,1-dialkyl-2-alkylisothioureas was accomplished in several ways. The most simple method was the treatment of the appropriate 3-(*O*,*O*-dialkylthiophosphoryl)-1,1-dialkyl-2-alkylisothioureas with alkyl iodides where good yields of compounds were obtained. However, for spectral and biological purposes, chromatographic purification was necessary.

The isomerization of 3-(*O*,*O*-dialkylthiophosphoryl)isothioureas and ureas, respectively by treatment with alkyl iodides could advantageously be followed by t.l.c. using DCQ for detection. The isomeric 3-(*O*,*S*-dialkylthiophosphoryl)isothioureas are more polar, have lower R_f values, and give different colour on detection with DCQ (yellow spots in contrast to brown spots of the starting 3-(*O*,*O*-dialkylthiophosphoryl)isothioureas). This fact is due to sulfur bound differently to phosphorus. In the case of thione sulfur (P = S) the colour is brown while in that of the thiol sulfur (P − S) it is yellow.

The structures of the prepared compounds were determined by i.r., u.v., and ^{1}H-n.m.r. spectrometry as well as by comparison with the spectra of model and similar compounds [1, 2, 4, 5].

In the i.r. spectra of the investigated compounds containing P = O group, strong bands ν(P = O) were observed in the region of 1212—1233 cm^{-1} (Table 2).

The bands in the region of 1584—1602 cm^{-1} prove the presence of the C = N bonds. In the spectra of compounds containing benzene or ethylene groups these bands are overlapped by the bands of ν(C = C).

In the u.v. spectra of the investigated compounds (Table 3) one to two intensive bands are observed which point to the presence of the conjugated system of bonds X = P − N = C. This is in accordance with our previous works dealing with similar compounds [1—4].

In the ^{1}H-n.m.r. spectra of the investigated compounds (Table 4) singlets of protons of the CH_3—N, CH_3—O, and CH_3—S groups were observed; the signals of protons of methoxy groups were observed at the lowest field. Triplets of protons of methyl groups in CH_3CH_2O— groups and multiplets of protons of methylene and methine groups were observed, too.

Table 2

Infrared spectral data of the studied compounds (in CCl_4)

Compound	$\tilde{\nu}/cm^{-1}$			
	ν(POC)	ν(P=O)	ν(C=N)	Other bands
II[a]	1041 1066		1582	544, 641, 668, 689, 821, 877, 953, 1124, 1182, 1256, 1377, 1403, 1433, 1475, 2842, 2943
III	1040	1233	1584	769, 930, 980, 1101, 1136, 1174, 1263, 1282, 1308, 1366, 1386, 1423, 1459, 2978, 2966
IV	1039 1062		1602	672, 891, 960, 1103, 1128, 1166, 1263, 1317, 1381, 1440, 1473, 2948, 2987
V	1033 1059		1596	669, 884, 951, 1092, 1122, 1161, 1259, 1311, 1436, 1467, 2930, 2974
VI	1041 1065		1602	671, 894, 960, 1107, 1131, 1171, 1266, 1386, 1443, 1475, 2948, 2986
VII[a,b]	1046		1590	521, 568, 608, 678, 801, 886, 931, 967, 988, 1094, 1124, 1234, 1385, 1434, 1476, 2936, 2995, 3025
IX[a]	1063		1600	970, 1125, 1260, 1385, 1436, 1476, 2901, 2932, 2979
X[a]	1036 1058		1586	529, 614, 633, 657, 834, 878, 896, 953, 973, 1099, 1118, 1158, 1218, 1270, 1297, 1353, 1386, 1410, 1443, 2866, 2905, 2978
XII	1030 1052		1583	650, 827, 873, 893, 949, 966, 1115, 1154, 1213, 1270, 1354, 1388, 1410, 1445, 2870, 2926, 2980
XVII	1051 996		1580	673, 869, 899, 939, 969, 1106, 1119, 1148, 1208, 1238, 1310, 1379, 1395, 1422, 1475, 1499, 2894, 2928, 2987
XXV[b]	1036		1600	693, 879, 950, 969, 1120, 1179, 1377, 1434, 2838, 2930
XXVII	1043	1233	1602	767, 884, 942, 968, 1128, 1269, 1310, 1385, 1441, 1473, 2948, 2990
XXVIII	1040	1214	1594	880, 960, 1120, 1263, 1376, 1402, 1436, 1466, 2928, 2968
XXIX[a]	1021	1214	1595	529, 565, 597, 652, 814, 879, 839, 962, 1099, 1122, 1160, 1241, 1263, 1291, 1311, 1375, 1433, 2874, 2932, 2967
XXXI[a]	1046 1060	1219	1600	711, 835, 888, 965, 1160, 1263, 1372, 1401, 1436, 1456, 2868, 2929, 2976
XXXII[a]	1040	1212	1584	500, 641, 702, 816, 851, 862, 932, 867, 1180, 1240, 1275, 1332, 1352, 1401, 1448, 1595, 2370, 2926, 2980

a) Measured on UR-20 spectrophotometer; *b*) measured in chloroform.

Table 3

Ultraviolet spectral data of the studied compounds (in methanol)

Compound	λ_{max} nm	log ε	λ_{max} nm	log ε
II	210	4.18	247.5	4.19
V	204.5	4.28	236.5	4.21
VI	212.5	3.85	237.5	4.09
VII	215	3.91	233	4.17
X	209	4.16	237.5	4.14
XII	212	3.69	243	4.02
XV	230	4.11	—	—
XXV	206	3.67	230	4.98
XXVI	230	4.21	—	—
XXVIII	232	4.23	—	—
XXIX	231	4.18	—	—
XXX	231	4.12	—	—
XXXII	203	4.09	237	4.22

None of the synthesized compounds showed so high insecticidal, acaricidal, and ovicidal activity as the standards Malathion, Fenitrothion, and Karbofenthion. The compound *XXV* was shown to be most active of this group of compounds, however, in contact insecticidal activity on *Musca domestica* was orderly less active than Fenitrothion; in time activity was almost so active (75%) as that of Fenitrothion. The acaricidal activity of this compound on *Tetranychus urticae* was approximately by one order lower than that of Karbofenthion. The ovicidal activity on *T. urticae* was much lower than that of the standard Karbofenthion. On the above-mentioned test objects, the compounds *IV*, *XV—XVIII*, and *XXIV* exhibited lower activity than the compound *XXV*. The fungicidal and the herbicidal activities of the prepared compounds in concentrations applied were not measurable.

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Table 4

^{1}H-NMR spectral data of the studied compounds (in $CDCl_3$)

Compound	δ (p.p.m.)					
II	CH_3N 3.11 (6H, s)	CH_3O 3.63 (6H, d)	Ph 7.32 (5H, m)			
X	CH_3CH_2 1.31 (6H, t)	CH_2CH_3 2.86 (4H, m)	CH_3N 3.23 (6H, s)	CH_2S 4.39 (2H, s)	Ph 7.32 (5H, m)	
XXX	CH_2CH_3 1.20—1.42	$CHCH_3$ (9H, m)	CHS 2.42 (1H, m)	CH_2S 3.07 (2H, m)	CH_3N 3.25 (6H, s)	CH_2O 3.95 (2H, m)
XXVI	CH_3CH_2 1.34 (3H, t)	CH_3S 2.54 (3H, s)	CH_2S 2.85 (2H, m)	CH_3N 3.25 (6H, s)	CH_3O 3.71 (3H, d)	

Observed multiplicities: s — singlet, d — doublet, t — triplet, m — multiplet.

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