Benzothiazole compounds XXVI. Synthesis of *S*-[1-acetyl-2-(2-oxobenzothiazol-3-yl)ethyl] *O,O*(*O,N*, *O,S*)-dialkyl thio(dithio)phosphates and *S*-[1-acetyl-2-(2-thioxobenzothiazol-3-yl)ethyl] *O,O*(*O,S*)-dialkyl thio(dithio)phosphates

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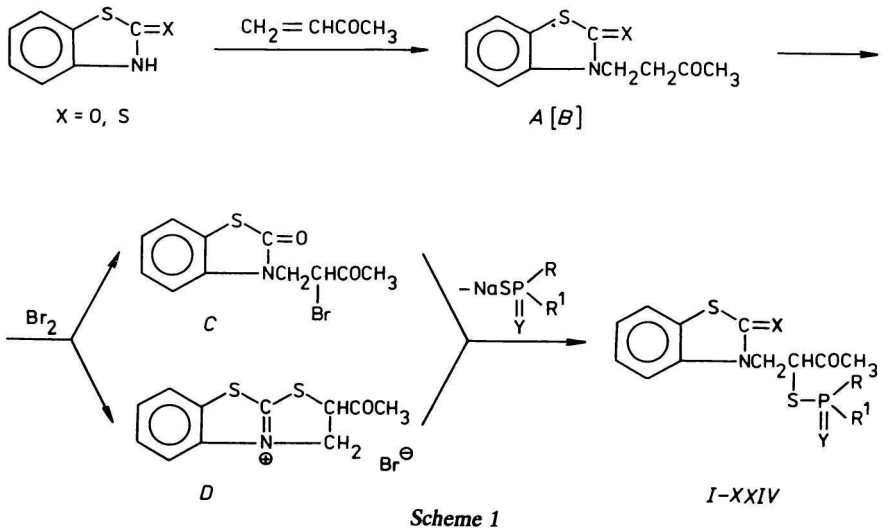
S-[1-Acetyl-2-(2-oxobenzothiazol-3-yl)ethyl] *O,O*(*O,N*, *O,S*)-dialkyl thio(dithio)phosphates have been prepared by treatment of 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone with salts of *O,O*(*O,N*, *O,S*)-dialkyl thio(dithio)phosphoric acids and *S*-[1-acetyl-2-(2-thioxobenzothiazol-3-yl)ethyl] *O,O*(*O,N*)-dialkyl thio(dithio)phosphates by treatment of 2,3-dihydro-2-acetylthiazolo[2,3-*b*]benzothiazolium bromide with salts of *O,O*(*O,N*)-dialkyl thio(dithio)phosphoric acids. The structures of the prepared compounds were proved by their ^{1}H NMR and IR spectra. It has been found that bromination of 3-(3-oxobutyl)-2-benzothiazolinethione resulted in 2,3-dihydro-2-acetylthiazolo[2,3-*b*]benzothiazolium bromide. The compounds at lower concentrations did not exhibit sufficiently high pesticidal activity.

S-[1-Ацетил-2-(2-оксобензотиазол-3-ил)этил]-*O,O*(*O,N O,S*)-диалкилтио(дитио)фосфаты были получены взаимодействием 3-(2-бром-3-оксобутил)-2-бензотиазолинона с солями *O,O*(*O,N O,S*)-диалкилтио(дитио)фосфорных кислот, а *S*-[1-ацетил-2-(2-тиоксобензотиазол-3-ил)этил]-*O,O*(*O,N*)-диалкилтио(дитио)фосфаты взаимодействием бромида 2,3-дигидро-2-ацетилтиазоло[2,3-*b*]бензотиазолия с солями *O,O*(*O,N*)-диалкилтио(дитио)фосфорных кислот. Структуры приготовленных соединений были подтверждены их ^{1}H ЯМР и ИК-спектрами. Обнаружено, что бромирование 3-(3-оксобутил)-2-бензотиазолинтиона вело к образованию бромида 2,3-дигидро-2-ацетилтиазоло[2-3-*б*]-бензотиазолия. В низких концентрациях полученные соединения не проявляли достаточно высокой пестицидной активности.

Organophosphoric compounds of benzothiazole have found extensive application in agriculture as herbicides, fungicides, insecticides, and acaricides [1—3].

The aim of our present work was to prepare 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone and 3-(2-bromo-3-oxobutyl)-2-benzothiazolinethione by bromination of 3-(3-oxobutyl)-2-benzothiazolinone and 3-(3-oxobutyl)-2-benzothiazolinethione, respectively, and treat these compounds with salts of *O,O*(*O,N*,

O,S)-dialkyl thio(dithio)phosphoric acids in order to obtain *S*-[1-acetyl-2-(2-oxobenzothiazol-3-yl)ethyl] *O,O*(*O,N*, *O,S*)-dialkyl thio(dithio)phosphates and *S*-[1-acetyl-2-(2-thioxobenzothiazol-3-yl)ethyl] *O,O*(*O,S*)-dialkyl thio(dithio)--phosphates according to Scheme 1.



Scheme 1

Alkylation of 2-hydroxybenzothiazole results in 3-alkyl-2-benzothiazolinones. Addition of methyl vinyl ketone occurs also at the position 3 under the formation of 3-(3-oxobutyl)-2-benzothiazolinone. Alkylation of 2-mercaptobenzothiazole in alkali medium takes place at the position 2 but addition of methyl vinyl ketone at the position 3. This difference has been explained by *Halasa* and *Smith* [4] on the basis of oxibase scale of ambident nucleophiles. Such a scale allows to predict conditions for formation of either N or S products. These authors carried out the reactions in THF using catalytic amount of NaH. We used CH_3OH as the reaction medium and catalytic amount of CH_3ONa. It was necessary to redistil and stabilize methyl vinyl ketone with hydroquinone prior to use.

3-(2-Bromo-3-oxobutyl)-2-benzothiazolinone (*C*) has been prepared by bromination of 3-(3-oxobutyl)-2-benzothiazolinone (*A*). Bromination proceeded best in CCl_4 where the product obtained was of highest purity. In benzene, chloroform, acetic acid or ethanol a mixture of derivatives was formed. Exactly one equivalent of bromine has to be used in the reaction, since its excess brings about a formation of 3-(2,4-dibromo-3-oxobutyl)-2-benzothiazolinone which is difficult to separate by crystallization. Successful bromination requires also sufficiently slow addition of bromine; the solution should be decolorized before further amount of bromine is

added. Otherwise, a mixture of mono- and disubstituted bromo derivatives is again obtained. The structure of 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone was proved by ^{1}H NMR spectra.

The composition of the compound formed on bromination of 3-(3-oxobutyl)--2-benzothiazolinethione (*B*) in chloroform pointed to monobromo derivative. On the basis of its high melting point (236—240 °C) and solubility in warm water we came to an assumption that cyclization had taken place under the formation of 2,3-dihydro-2-acetylthiazolo[2,3-*b*]benzothiazolium bromide (*D*) which has not been synthesized so far. We explain this process by formation of intermediate 3-(2-bromo-3-oxobutyl)-2-benzothiazolinethione where a covalent bond may be formed between the nucleophilic sulfur in the side chain on C-2 bearing both bromine and carbonyl group. The structure was proved by evaluation of the ^{1}H NMR spectra. Cyclic benzothiazolium salts, known so far, have been synthesized from various 2-haloalkylthiobenzothiazoles.

S-[1-Acetyl-2-(2-oxobenzothiazol-3-yl)ethyl] *O,O*-dialkyl thio(dithio)phosphates (*I*, *III—V*, *VIII*, *X*, *XII*, *XIV*, *XVI*, *XVII*, *XX*, *XXII*, *XXIV*) were prepared by the reaction of 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone with salts of *O,O*-dialkyl thio(dithio)phosphoric acids, prepared according to [5, 6]. The reaction proceeded at room temperature and 2-butanone was found to be the most suitable reaction medium, since both starting compounds are soluble in it. We have compared the reaction rates of sodium *O,O*-diethyl dithiophosphate in acetonitrile and of free acid in chloroform, respectively, with 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone (IR region). The results are in agreement with nucleophility of acids and their salts. The rate constant for nucleophilic substitution of bromine with sodium *O,O*-diethyl dithiophosphate was $2.48 \times \times 10^{-3}$ dm^3 mol^{-1} s^{-1}. The rate constant for the reaction of the bromo derivative with acid was 7.99×10^{-4} dm^3 mol^{-1} s^{-1}. Though the reactions were studied in different solvents, the rate constant values clearly indicated that the reaction of acid with bromo derivative was three times slower than that with its salt. The synthesized derivatives, isolated from aqueous medium and purified chromatographically, are yellow oily compounds. Their properties are presented in Table 1.

S-[1-Acetyl-2-(2-thioxobenzothiazol-3-yl)ethyl] *O,O*-dialkyl thio(dithio)phosphates (*II*, *VI*, *VII*, *XIII*, *XV*, *XVIII*, *XIX*, *XXIII*) were prepared by treatment of 2,3-dihydro-2-acetylthiazolo[2,3-*b*]benzothiazolium bromide with salts of *O,O*--dialkyl thio(dithio)phosphoric acids. We assume that the nucleophilic reaction proceeded on C-2 of the thiazole ring where the acetyl group was located. The electron deficit on this carbon is, due to the carbonyl group, higher than that on carbon in the position 2 of the benzothiazole ring, since electron deficit is not localized on nitrogen but spread out over the whole benzothiazole skeleton, or

Table1
Characterization of the synthesized compounds

Compound	R	R¹	X	Y	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.	n(D, 20 °C)
							C	H	N	P	%	°C	
I	OCH_3	OCH_3	O	S	$C_{13}H_{16}NO_4PS_3$	377.44	41.37 41.00	4.27 4.09	3.71 3.70	8.21 8.06	90		1.6108
II	OCH_3	OCH_3	S	S	$C_{13}H_{16}NO_3PS_4$	393.50	39.68 39.92	4.10 4.29	3.56 3.27	7.87 7.49	80		*
III	OC_2H_5	OC_2H_5	O	O	$C_{15}H_{20}NO_5PS_2$	389.43	45.26 44.96	5.18 5.01	3.60 3.72	7.95 7.62	87		1.5800
IV	OC_2H_5	OC_2H_5	O	S	$C_{15}H_{20}NO_4PS_3$	405.19	44.46 44.44	4.98 4.94	3.46 3.45	7.64 7.90	80		1.5939
V	C_2H_5	OC_2H_5	O	S	$C_{15}H_{20}NO_3PS_3$	389.49	46.26 45.93	5.18 5.25	3.60 4.42	7.95 8.19	82		1.6050
VI	OC_2H_5	OC_2H_5	S	S	$C_{15}H_{20}NO_3PS_4$	421.56	42.74 42.60	4.78 4.70	3.32 3.30	7.35 7.58	93	67—69	
VII	OC_2H_5	OC_2H_5	S	O	$C_{15}H_{20}NO_4PS_3$	405.49	44.43 44.63	4.97 5.11	3.45 3.52	7.64 7.91	61	88—90	
VIII	OC_2H_5	OC_3H_7-i	O	O	$C_{16}H_{22}NO_5PS_2$	403.45	47.63 47.44	5.50 5.45	3.47 3.47	7.68 7.50	84		1.5660
IX	OC_2H_5	NHC_3H_7-i	O	O	$C_{16}H_{23}N_2O_4PS_2$	402.47	47.75 47.75	5.76 5.63	6.96 6.71	7.70 7.44	85		*
X	SC_2H_5	OC_4H_9-i	O	O	$C_{17}H_{24}NO_4PS_3$	433.55	47.10 46.80	5.58 5.31	3.23 3.30	7.14 7.00	80		1.5670
XI	OC_2H_5	NHC_3H_7-i	S	S	$C_{16}H_{23}N_2O_3PS_3$	418.53	45.92 45.96	5.54 5.56	6.69 6.49	7.40 7.76	36	137—139	
XII	OC_3H_7	OC_3H_7	O	O	$C_{17}H_{24}NO_5PS_2$	417.47	48.91 48.63	5.79 5.67	3.36 3.33	7.42 7.42	92		1.5562

Table 1 (Continued)

Compound	R	R[1]	X	Y	Formula	M_r	w_i(calc.)/% / w_i(found)/%				Yield	M.p.	n(D, 20 °C)
							C	H	N	P	%	°C	
XIII	OC_3H_7	OC_3H_7	S	O	$C_{17}H_{24}NO_4PS_3$	433.55	47.10 46.90	5.58 5.81	3.23 3.10	7.14 7.31	84		1.5889
XIV	OC_3H_7-i	OC_3H_7-i	O	O	$C_{17}H_{24}NO_5PS_2$	417.48	48.91 48.64	5.79 5.48	3.36 3.34	7.42 7.34	92		1.5489
XV	OC_3H_7-i	OC_3H_7-i	S	O	$C_{17}H_{24}NO_4PS_3$	433.55	47.10 46.81	5.58 5.47	3.23 3.27	7.14 7.02	90	98—100	
XVI	OC_3H_7-i	OC_3H_7-i	O	S	$C_{17}H_{24}NO_4PS_3$	433.55	47.10 46.83	5.58 5.39	3.23 3.15	7.14 7.31	94		1.5750
XVII	$OCH_2CH{=}CH_2$	$OCH_2CH{=}CH_2$	O	O	$C_{17}H_{20}NO_5PS_2$	413.44	49.39 49.51	4.88 4.70	3.39 3.47	7.49 7.41	90		1.5855
XVIII	$OCH_2CH{=}CH_2$	$OCH_2CH{=}CH_2$	S	O	$C_{17}H_{20}NO_4PS_3$	429.51	47.54 47.20	4.69 4.91	3.26 3.02	7.21 7.00	88		1.5768
XIX	OC_4H_9	OC_4H_9	S	O	$C_{19}H_{28}NO_4PS_3$	461.60	49.44 49.61	6.11 6.02	3.03 3.23	6.71 6.37	84		1.5820
XX	OC_4H_9	OC_4H_9	O	O	$C_{19}H_{28}NO_5PS_2$	445.51	51.21 50.95	6.28 6.28	3.14 3.08	6.96 7.05	89		1.5495
XXI	OC_4H_9-*sec.*	OC_4H_9-*sec.*	O	O	$C_{19}H_{28}NO_5PS_2$	445.51	51.21 50.98	6.28 6.21	3.14 3.12	6.96 6.96	88		1.5488
XXII	OC_4H_9-i	OC_4H_9-i	O	O	$C_{19}H_{28}NO_5PS_2$	445.51	51.21 51.13	6.28 6.19	3.14 3.11	6.96 7.00	83		1.5458
XXIII	OC_4H_9-i	OC_4H_9-i	S	O	$C_{19}H_{28}NO_4PS_3$	461.60	49.44 49.13	6.11 5.92	3.03 3.16	6.71 6.64	78	88—89	
XXIV	OC_4H_9-i	OC_4H_9-i	O	S	$C_{19}H_{28}NO_4PS_3$	461.60	49.44 49.19	6.11 6.19	3.03 3.03	6.71 6.92	88		1.5661

* Coloured viscous liquid.

even on methylene group of the thiazole ring similarly as it was proved by the X-ray structure of 3-benzylbenzothiazolium bromide.

The structures of the synthesized compounds were confirmed also by evaluation of their IR spectra. The absorption bands of medium intensity in the region of $\tilde{\nu} = 1230$—$1270\ cm^{-1}$ proved the presence of the stretching P=O vibrations while the bands at $\tilde{\nu} = 570$—$670\ cm^{-1}$ belonged to P=S vibrations (Table 2). It can be seen that the wavenumbers of the bands ascribed to P=O and P=S groups changed in dependence on the alkoxy group. With the increasing number of C in the chain the position of the band shifted to lower wavenumbers, however, the band intensity did not change. The IR spectra revealed that the compound *IX* was a mixture of P=O and P=S isomers which we failed to separate chromatographically. The derivatives *IX* and *XI* were synthesized for comparative purposes in biological tests.

Table 2

Effect of the substituents R, R^1 on the wavenumber ($\tilde{\nu}/cm^{-1}$) of the P=Y group of the synthesized compounds

Compound	ν(P=O)	ν(P=S)	Compound	ν(P=O)	ν(P=S)
I		655	*XIII*	1240	
II		660	*XIV*	1250	
III	1270		*XV*	1240	
IV		650	*XVI*		630
V		640	*XVII*	1270	
VI		650	*XVIII*	1230	
VII	1245		*XIX*	1235	
VIII	1260		*XX*	1250	
IX	1235	570	*XXI*	1250	
X	1240		*XXII*	1250	
XI		590	*XXIII*	1240	
XII	1265		*XXIV*		570

The tests for contact and systemic insecticidal activity on *Musca domestica*, *Calandra granaria*, and *Aphis fabae* showed that the activities with the synthesized compounds were lower than that of Metation. Likewise, acaricidal activities were lower than that of Akarition. The compounds *III*, *VII*, *IX*, *XIV*, *XVII*, *XX*, and *XXIV* at $\delta = 5000$ ppm and 500 ppm exhibited acaricidal-ovicidal activity on eggs of *Tetranychus urticae*. The biological tests were carried out at the Research Institute of Agrochemical Technology.

Experimental

Characterization of the synthesized compounds is presented in Table 1. ^1H NMR spectra were measured in $CDCl_3$ and F_3CCOOD on a Tesla 487 apparatus at 80 MHz using

hexamethyldisiloxane as internal standard. IR spectra were measured in $CHCl_3$ on a Perkin—Elmer 180 spectrophotometer. Column chromatography was performed on silica gel L 40/100 using methanol—benzene (volume ratio = 1 : 4) as the eluent.

3-(3-Oxobutyl)-2-benzothiazolinone (A)

2-Benzothiazolinone (30.2 g; 0.2 mol) was dissolved in dry methanol (120 cm^3) and after addition of sodium (0.5 g), methyl vinyl ketone (15 g; 0.25 mol) was added dropwise. The reaction mixture was stirred until crystallization of the product began. Then it was allowed to stand for 2 h and the product was purified by crystallization from ethanol. Yield = 90 %, m.p. = 113—115 °C.

For $C_{11}H_{11}NO_2S$ (M_r = 221.27) w_i(calc.): 14.47 % S, 6.33 % N; w_i(found): 14.72 % S, 6.41 % N. ^1H NMR (δ/ppm): 7.0—7.5 (ar, 4H, m), 4.15 (CH_2, 2H, t), 2.90 (CH_2CO, 2H, t), 2.17 (CH_3, 3H, s).

3-(3-Oxobutyl)-2-benzothiazolinethione (B)

2-Mercaptobenzothiazole (16.7 g; 0.1 mol) was dissolved in dry methanol (60 cm^3) with stirring at 40 °C and after addition of sodium (0.2 g), methyl vinyl ketone (10 g; 0.15 mol) was added dropwise. The reaction mixture was stirred at 60 °C for 1 h. After cooling the solid portion was crystallized from ethanol. Yield = 75 %, m.p. = 139—140 °C.

For $C_{11}H_{11}NOS_2$ (M_r = 237.34) w_i(calc.): 27.04 % S, 5.91 % N; w_i(found): 27.02 % S, 5.88 % N. ^1H NMR (δ/ppm): 7.1—7.6 (ar, 4H, m), 4.65 (CH_2, 2H, t), 3.0 (CH_2CO, 2H, t), 2.20 (CH_3, 3H, s).

3-(2-Bromo-3-oxobutyl)-2-benzothiazolinone (C)

3-(3-Oxobutyl)-2-benzothiazolinone (22.1 g; 0.1 mol) was dissolved in CCl_4 (100 cm^3) and under stirring and cooling with water, bromine (16 g; 0.1 mol), diluted with CCl_4 (20 cm^3), was added dropwise at such a rate that the solution decolorized continually. Then the reaction mixture was stirred for 1 h and the solid portion was crystallized from ethanol. Yield = 90 %, m.p. = 117—118 °C.

For $C_{11}H_{10}BrNO_2S$ (M_r = 300.18) w_i(calc.): 26.62 % Br, 4.28 % N; w_i(found): 26.14 % Br, 4.50 % N. ^1H NMR (δ/ppm): 7.0—7.5 (ar, 4H, m), 4.95 (CH, 1H, dd), 4.06—4.75 (CH_2, 2H, m), 2.40 (CH_3, 3H, s).

2,3-Dihydro-2-acetylthiazolo[2,3-b]benzothiazolium bromide (D)

3-(3-Oxobutyl)-2-benzothiazolinethione (23.7 g; 0.1 mol) was dissolved in dry chloroform (100 cm^3) and bromine (16 g; 0.1 mol) was added dropwise under stirring at room temperature at such a rate that the solution decolorized continually. The precipitate, a light-green salt of the product, was washed with ethanol thoroughly. Yield = 80 %, m.p. = 236—240 °C.

For $C_{11}H_{10}BrNOS_2$ ($M_r = 316.24$) w_i(calc.): 25.31 % Br, 4.43 % N; w_i(found): 25.62 % Br, 4.29 % N. ^{1}H NMR (δ/ppm): 7.25—7.75 (ar, 4H, m), 5.45 (CH, 1H, dd), 5.27 (CH_2, 1H, dd), 4.72 (CH_2, 1H, dd), 2.17 (CH_3, 3H, s).

S-[1-Acetyl-2-(2-oxobenzothiazol-3-yl)ethyl] O,O-dimethyl dithiophosphate (I)

Into the solution of sodium *O,O*-dimethyl dithiophosphate (7.2 g; 0.04 mol) in butanone (50 cm^3) the solution of 3-(2-bromo-3-oxobutyl)-2-benzothiazolinone (10.5 g; 0.035 mol) in butanone (50 cm^3) was added and the reaction mixture was stirred at room temperature for 3 h. Then it was poured into water (150—200 cm^3) containing NaCl (10—15 g). The product was extracted with ether, dried with Na_2SO_4 and the oily residue was purified on silica gel using methanol—benzene (volume ratio = 1 : 4) as eluent. The compounds *I, III, V, VIII—X, XII, XIV, XVI, XVII, XX—XXII,* and *XXIV* were prepared in a similar way.

S-[1-Acetyl-2-(2-thioxobenzothiazol-3-yl)ethyl] O,O-dimethyl dithiophosphate (II)

2,3-Dihydro-2-acetylthiazolo[2,3-*b*]benzothiazolium bromide (12.5 g; 0.04 mol) was dissolved in butanone (50 cm^3) to which the solution of sodium *O,O*-dimethyl dithiophosphate (7.2 g; 0.04 mol) in butanone (50 cm^3) was added. The reaction mixture was heated to reflux and then stirred at room temperature for 3 h. After pouring the reaction mixture into water (150 cm^3) containing NaCl (15 g), the product was extracted with chloroform, dried with Na_2SO_4, and purified chromatographically on silica gel using methanol—benzene (volume ratio = 1 : 4) as eluent. The compounds *XIII, XVIII,* and *XIX* were prepared similarly. The compounds *VI, VII, XI, XV,* and *XXIII* were crystallized from ethanol. ^{1}H NMR (δ/ppm) for *VI*: 7.15—7.5 (ar, 4H, m), 4.5—5.25 (CH_2—CH, 3H, m), 3.97 (($O—CH_2)_2$, 4H, q), 2.40 ($COCH_3$, 3H, s), 1.25 (($CH_3)_2$, 6H, t).

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