Russian Journal of General Chemistry, Vol. 73, No. 4, 2003, pp. 638–642. Translated from Zhurnal Obshchei Khimii, Vol. 73, No. 4, 2003, pp. 676–680.

Reaction of Potassium Salts of *N*-(Thio)phosphorylthioamides with Chlorinated 1,3,5-Triazines

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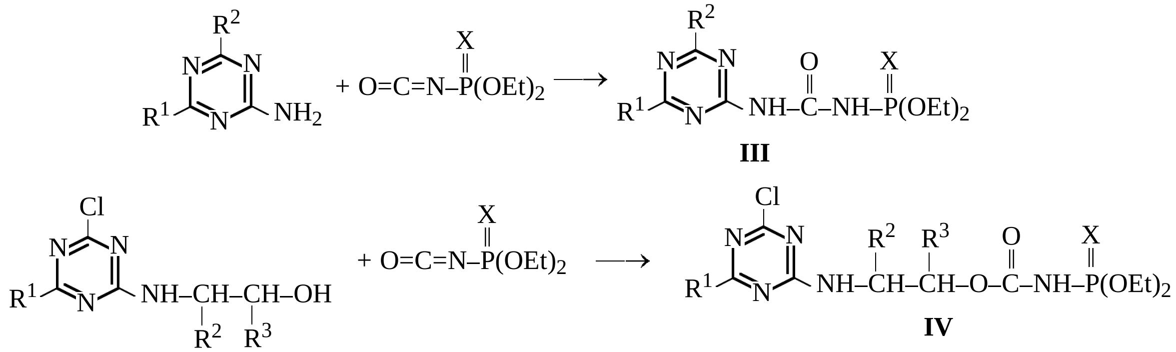
Received March 23, 2001

Abstract—Potassium salts of *N*-(thio)phosphorylthioamides can substitute one, two, or three halogen atoms in chlorinated 1,3,5-triazine molecules to give the products of imidothiyl structure. At low temperature, products of incomplete substitution of halogen in the starting 1,3,5-triazines can be obtained.

We have shown previously [1, 2] that N-(thio)-phosphorylated thioamides and their potassium salts are readily and selectively alkylated with alkyl halides with the transfer of the reaction center to the sulfur atom of the thiocarbonyl group, which allows preparation of a great variety of various S-functionalized derivatives of *N*-(thio)phosphorylthioamides [3–5]. This induced us to study substitution of chlorine atoms at the sp^2-hybridized carbon atom in chlorinated derivatives under the action of potassium salts **II** with the aim to obtain compounds exhibiting high biological activity due to the presence of the 1,3,5-triazine ring and *N*-(thio)phosphorylimidothioate group, the groups with pronounced potential biogenic properties. Synthesis of 1,3,5-triazine derivatives containing *N*-thiophosphorylurea or carbamate fragment was reported previously. These compounds were prepared by the reaction of bis- or monoamino-substituted derivatives of 1,3,5-triazine [6] or hydroxy-substituted derivatives of ethylamino- and ethylhydrazino-1,3,5-triazine [7] with phosphoryl isocyanates.



III

IV

The resulting substituted ureas **III** and urethanes **IV**, as well as their isothiouronium salts, exhibit high herbicidal activity [8–10].

We studied the reactions of potassium salts of *N*-diisopropoxythiophosphorylthiobenzamide **IIa** (X = S) and *N*-diisopropoxyphosphorylthiobenzamide **IIb** (X = O) with 2,4,6-trichloro-1,3,5-triazine (cyanuric acid chloride) **V**, 2-methoxy-4,6-dichloro-1,3,5-triazine **VI**, and 2,4-dimethoxy-6-chloro-1,3,5-triazine **VII**, which readily occur in anhydrous acetone or dioxane. The products were purified by passing through a column packed with alumina (Brockmann grade II). The IR and ^{31}P NMR data for the compounds obtained are listed in the table.

The reactions of potassium salts of *N*-diisopropoxy(thio)phosphorylthiobenzamide with cyanuric acid chloride **V** may yield mono-, di-, and trisubstituted products **VIII**–**X**. When performed at 0°C at the 1:1 ratio of the starting compounds, the reaction yielded disubstituted cyanuric acid chloride derivatives. The

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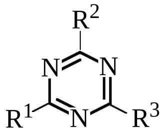
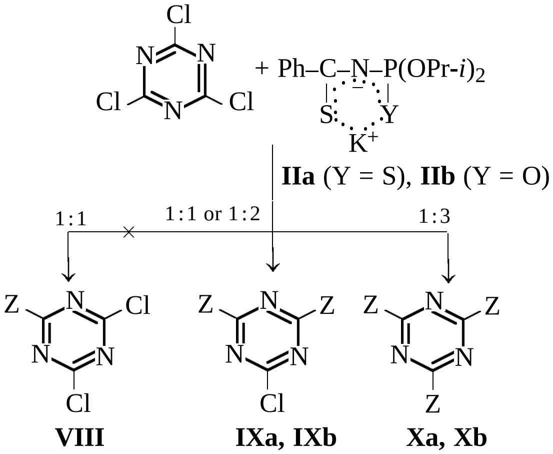
Spectral and physical characteristics of imidoyl-substituted 1,3,5-triazines **IX**–**XIV**



Comp. no.	R^1	R^2	R^3	Yield, %	n_D^{20}	IR spectrum, ν, cm^{-1}				^{31}P NMR spectrum, J_P, ppm
						P=X	POC	triazine	C=N	
IXa	Z^1 [a]	Z^1	Cl	78.0	1.5764	620, 650 w	1010–1070 br.v.s, 1110	1540, 1560	1620	56
IXa[b]	Z^1	Z^1	Cl	74.6	1.5770	620, 650 w	1010–1070 br.v.s, 1110	1540, 1560	1620	56
IXb	Z^2	Z^2	Cl	61.0	1.6804[c]	1245	970–1000 br.v.s	1550 br.s	1615	–8
Xa	Z^1	Z^1	Z^1	57.4	1.5970	620–650 br.w	980–1070 br.v.s, 1120	1540, 1560	1620	56
Xb	Z^2	Z^2	Z^2	49.0	1.6428	1245	1000–1070 br.v.s, 1120	1540, 1560	1620	–3
XI	OCH_3	Z^1	Cl	63.0	1.6373	620–655 br.w	1000–1070 br.v.s, 1120	1560, 1540 vs.s	1620 s	62
XII	OCH_3	Z^1	Z^1	58.0	–[d]	620 br.w	960–1000 br.v.s, 1100	1525, 1500 vs.s	1660 s	54
XIII[e]	OCH_3	Z^1	OH	10.0	–[d]	625, 650 w	1000, 1010	1550 br.s	1675	54
XIV	OCH_3	OCH_3	Z^1	24.0	–[d]	625 br.w	980–1000	1560 br.s	1610	58

[a] Z^1 = S–C(Ph)=N–P(S)(O–Pr-*i*)$_2$; Z^2 = S–C(Ph)=N–P(O)(OPr-*i*)$_2$. [b] The product was isolated from the reaction of cyanuric acid chloride with the potassium salt of thioamide **IIa** in 1 : 1 molar ratio. Yield based on **IIa**. [c] The refractive index was measured at 25°C. [d] The refractive undex could not be measured. [e] ν(NH/OH) 3100–3400 cm^{-1}, br.

resulting bright violet liquid products were identified by IR and ^{31}P NMR spectroscopy and elemental analysis as *N*-(thio)phosphorylthiobenzimidates **IX**. When performed at the 1 : 3 ratio of the starting products with refluxing, the reaction yielded trisubstituted products **X**. These compounds are dark red liquids. The structures of compounds **X** and their compositions were determined spectroscopically (see table) and by elemental analysis.



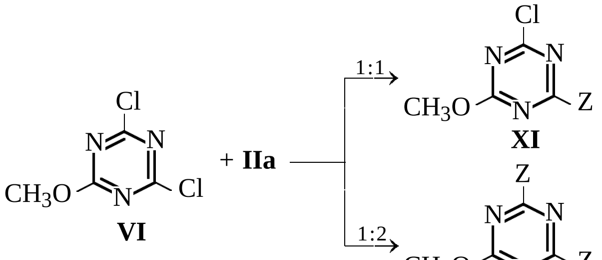
Z = S–C(Ph)=N–P(S)(OPr-*i*)$_2$ (**a**),
S–C(Ph)=N–P(O)(OPr-*i*)$_2$ (**b**).

Potassium salts of *N*-(thio)phosphorylthiobenzamides react with cyanuric acid chloride with the participation of the thiocarbonyl atom to give the products of the imidothiyl structure, which is confirmed by the presence in the IR spectra of **IX** and **X** of the absorption band at 1600–1675 cm^{-1}, characteristic of the stretching vibrations of the C=N bond. The ^{31}P NMR signals in these compounds are observed at –8 (**IXb**) and –3 ppm (**Xb**), or at 56 ppm (**IXa**, **Xa**), which indicates that the corresponding compounds have the amidophosphate (X = O) or amidothiophosphate (X = S) structure.

A more complex pattern was observed in the reaction of salt **IIa** with mono- and dimethoxy derivatives of cyanuric acid chloride. Introduction of one or two electron-donating methoxy groups negatively affects the stability of the resulting products. The reaction with methoxy derivative **VI** is nonselective and yields a mixture of products susceptible to hydrolysis, which complicates their separation. The ^{31}P NMR spectrum of the reaction mixture, along with the signals indicative of the amidophosphate surrounding of phosphorus, contains the signals of by-products of unknown structure at 71 and 86 ppm. Formation of these compounds presumably involves migration of the thiophosphoryl group, but we failed to identify these compounds and to elucidate the reaction pathway. We isolated and characterized only the products of chlorine substitution having the imidothiyl structure.

The reaction of thioamide **IIa** with 2-methoxy-4,6-dichloro-1,3,5-triazine **VI** at room temperature leads to the substitution of one chlorine atom. The product **XI** isolated by passing through the column packed with alumina contains a singlet at 62 ppm in the ^{31}P NMR spectrum, indicative of the amidothiophosphate structure. The absorption bands of triazine and imidothiyl fragments (ν, cm^{-1}) are observed at 1620 v.s (C≡N), 1560, 1540 v.s (triazine), 1000–1070, 1120 br.v.s (POC), and 620–655 br.w (P=S). These data confirm the structure of the product. The N–H absorption band at 3000–3400 cm^{-1} is absent.

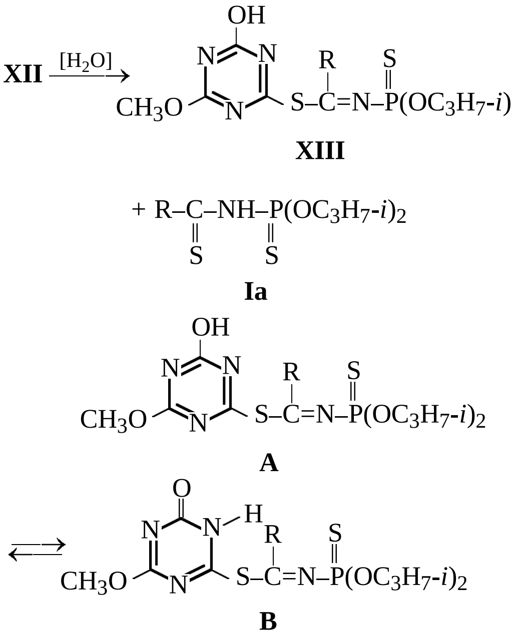
Heating of dichloride **VI** with two equivalents of potassium salt **IIa** leads to the substitution of two chlorine atoms in the starting triazine. By column chromatography on alumina, we isolated 2-methoxy-4,6-(*S*-isothiobenzamido-*N*-diisopropoxythiophosphoryl)-1,3,5-triazine **XII**. Its IR spectrum contains the absorption bands (ν, cm^{-1}) at 1660 v.s (C=N), 1525, 1500 v.s (triazine), 960–1000, and 1100 br.v.s (POC). The N–H absorption band at 3000–3400 cm^{-1} is absent. The signal at 54 ppm in the ^{31}P NMR spectrum confirms the structure of amidothiophosphate and, similarly to the above-mentioned cases, suggests the occurrence of the reaction at the sulfur atom of the C=S group.



VI **XI** **XII**

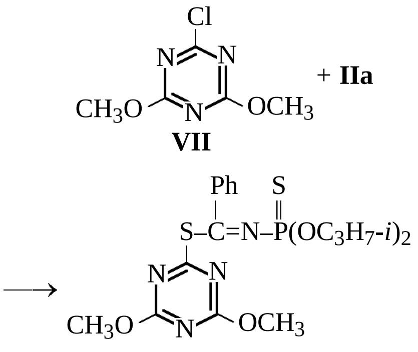
Z = S–C(Ph)=N–P(S)(OPr-i)$_2$.

We have found that the disubstituted product is hydrolytically unstable. Elution with acetone from the column packed with alumina gives 2-methoxy-4-(*N*-diisopropoxythiophosphoryl-*S*-thiobenzimidoyl)-6-hydroxy-1,3,5-triazine **XIII** as a cherry red oil with δ_P 54 ppm. The presence of the absorption bands at 1725 cm^{-1} related to C=O vibrations and of the band at 1675 cm^{-1} related to the C=N group suggests the presence of two tautomeric forms **A** and **B** of the hydrolysis product **XIII**. Also, the IR spectrum contains the bands of the other functional groups (ν, cm^{-1}): 3100–3400 br (OH, NH), 1550–1570 (triazine), 1000, 1010 (POC), 625, 650 w (P=S). Evidenly, compound **XIII** is formed by the reaction of disubstituted triazine **XII** with water adsorbed on alumina.



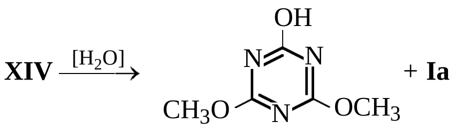
XIII **Ia** **A** **B**

The reaction of 2,4-dimethoxy-6-chloro-1,3,5-triazine **VII** with the potassium salt of *N*-diisopropoxythiophosphorylthiobenzamide **IIa** occurs in refluxing acetone and gives 2,4-dimethoxy-6-(*S*-isothiobenzamido-*N*-diisopropoxythiophosphoryl)-1,3,5-triazine **XIV** in a relatively low yield (24%). Its IR and ^{31}P NMR spectra are consistent with the suggested structure (see table).



VII **XIV**

Under the action of atmospheric moisture, phosphorus-containing dimethoxytriazine **XIV** decomposes to form *N*-diisopropoxythiophosphorylthiobenzamide **Ia** and 2,4-dimethoxy-6-hydroxy-1,3,5-triazine **XV** whose structure was confirmed by IR spectroscopy. Thioamide **Ia** was isolated from the reaction mixture and characterized spectroscopically; its structure was confirmed by coincidence of its constants with the published data [11].



XV

The lability of imidothiyl derivatives of 1,3,5-triazine **IX**–**XIV**, as compared to the previously studied imidothiotates, may be due to the fact that the carbon atom in 1,3,5-triazine is subjected to a strong electron-accepting effect of the neighboring nitrogen atom, and in its properties it resembles acyl rather than alkyl carbon atom.

We also attempted to perform the reaction of thioamides **I** and their salts with acyl halides, but these reactions are nonselective and yield numerous products (up to 10 signals are observed in the ^{31}P NMR spectrum); we failed to isolate them pure and characterize. Note that the ^{31}P NMR spectrum contains strong signals at 71 and 86 ppm, which were also observed in the reaction of salts **II** with compounds **VI** and **VII**.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-80 spectrometer for liquid films and mulls in mineral oil in the range 400–3700 cm^{-1}. The ^{31}P NMR spectra were measured on a KGU-4 custom-made NMR spectrometer (8 MHz) against external 85% phosphoric acid.

Reaction of potassium salt of *N*-diisopropoxyphosphorylthiobenzamide IIa with 2,4,6-trichloro-1,3,5-triazine V in 1 : 1 ratio. A solution of 7.12 g of potassium amide **IIa** in 30 ml of anhydrous acetone was slowly added dropwise with vigorous stirring at 0°C to a solution of 3.69 g of cyanuric acid chloride **V** in 50 ml of anhydrous acetone. The reaction mixture was allowed to stand at room temperature for 8 h, the KCl precipitate was filtered off, and the solvent was removed in a water-jet-pump vacuum. The residue was dissolved in hexane and thrice chromatographed on 50 g of neutral alumina (Brockmann grade II), and then the solvent was removed. 2-Chloro-4,6-bis(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-1,3,5-triazine **IX**, 5.57 g, was obtained as a dark red liquid, n_D^{20} 1.5770, δ_P 56 ppm. Yield 75% based on **IIa**. Found, %: C 46.02; H 5.04; P 8.29. $C_{29}H_{38}\cdot N_5ClO_4P_2S_4$. Calculated, %: C 46.67; H 5.09; P 8.32.

Reaction of potassium salt of *N*-diisopropoxythiophosphorylthiobenzamide IIa with 2-methoxy-4,6-dichloro-1,3,5-triazine VI in 1 : 1 molar ratio. A solution of 3.56 g of **IIa** in 100 ml of anhydrous acetone was slowly added dropwise with vigorous stirring to a solution of 1.80 g of 2-methoxy-4,6-dichloro-1,3,5-triazine in 50 ml of anhydrous acetone. The reaction mixture was allowed to stand at room temperature for 8 h, the KCl precipitate was filtered off, and solvent was removed in a water-jet-pump vacuum. The residue was dissolved in carbon tetrachloride and thrice chromatographed on 40 g of neutral alumina (Brockmann grade II). Then the solvent was removed, and 2.90 g (63%) of 2-methoxy-4-chloro-6-(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-1,3,5-triazine **XI** was obtained; n_D^{20} 1.6373, δ_P 62 ppm. Found, %: C 44.11; H 4.69; P 6.54. $C_{17}H_{22}ClN_4O_3PS_2$. Calculated, %: C 44.29; H 4.70; P 6.73.

Reaction of potassium salt of *N*-diisopropoxythiophosphorylthiobenzamide IIa with 2,4-dimethoxy-6-chloro-1,3,5-triazine VII. A solution of 3.56 g of **IIa** in 50 ml of absolute dioxane was slowly added dropwise with vigorous stirring to a solution of 1.76 g of 2,4-dimethoxy-6-chloro-1,3,5-triazine **VII** in 50 ml of absolute dioxane. The mixture was refluxed for 0.5 h, the KCl precipitate was filtered off, and the solvent was removed in a water-jet-pump vacuum. The residue was dissolved in carbon tetrachloride and thrice chromatographed on 40 g of neutral alumina (Brockmann grade II). The solvent was removed, and 1.1 g (24%) of 2,4-dimethoxy-6-(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-1,3,5-triazine **XIV** was obtained, δ_P 58 ppm.

Reaction of potassium salt of *N*-diisopropoxythiophosphorylthiobenzamide IIa with 2-methoxy-4,6-dichloro-1,3,5-triazine VI in 1 : 2 ratio. A solution of 11.1 g of **IIa** in 50 ml of absolute dioxane was slowly added dropwise with vigorous stirring to a solution of 1.80 g of 2-methoxy-4,6-dichloro-1,3,5-triazine in 50 ml of absolute dioxane. The reaction mixture was refluxed for 1 h, the KCl precipitate was filtered off, the solvent was removed in a water-jet-pump vacuum, and the residue was dissolved in benzene and thrice chromatographed on 40 g of neutral alumina (Brockmann grade II). Then the solvent was removed, and 4.3 g (58%) of 2,4-(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-6-methoxy-1,3,5-triazine

XII was obtained as a viscous reddish brown oil, δ_P 54 ppm. Found, %: C 48.40; H 5.32; P 8.40. $C_{30}H_{41}\cdot N_5O_5S_4P_2$. Calculated, %: C 48.53; H 5.53; P 8.36. The alumina was repeatedly washed with acetone. After removing the solvent, 0.4 g (10%) of 2-(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-4-hydroxy-6-methoxy-1,3,5-triazine **XIII** was obtained as a red oil, δ_P 54 ppm.

Reaction of potassium salts of *N*-(thio)phosphorylthiobenzamides IIa and IIb with cyanuric acid chloride in 1 : 2 ratio (*general procedure*). A solution of 0.02 mol of potassium salt of *N*-(thio)phosphorylthiobenzamide **IIa** or **IIb** in 50 ml of anhydrous acetone was slowly added dropwise with vigorous stirring to a solution of 1.84 g of **V** in 30 ml of anhydrous acetone. The mixture was refluxed for 15 min and allowed to stand at room temperature for 8 h. The KCl precipitate was filtered off, and the solvent was removed in a water-jet-pump vacuum. The residue was extracted with hexane, and the solvent was removed.

2,4-Bis(*N*-diisopropoxythiophosphorylthiobenzimidoyl)-6-chloro-1,3,5-triazine IXa. Yield 5.80 g (78%), n_D^{20} 1.5764, δ_P 56 ppm. Found, %: C 46.12; H 5.04; P 8.29. $C_{29}H_{38}ClN_5O_4P_2S_4$. Calculated, %: C 46.67; H 5.09; P 8.32.

2,4-Bis(*N*-diisopropoxyphosphorylthiobenzimidoyl)-6-chloro-1,3,5-triazine IXb. Yield 4.36 g (61%), n_D^{25} 1.6804, δ_P –8 ppm. Found, %: C 48.30; H 5.21; P 8.65. $C_{29}H_{38}ClN_5O_6P_2S_2$. Calculated, %: C 48.73; H 5.32; P 8.67.

Reaction of potassium salts of *N*-(thio)phosphorylthiobenzamides IIa and IIb with cyanuric acid chloride in 1 : 3 ratio (*general procedure*). A solution of 0.03 mol of potassium salt of *N*-(thio)phosphorylthiobenzamide **IIa** or **IIb** in 70 ml of anhydrous acetone was slowly added dropwise with vigorous stirring to a solution of 1.84 g of cyanuric acid chloride **V** in 30 ml of anhydrous acetone. The reaction mixture was refluxed for 4 h, the KCl precipitate was filtered off, and the solvent was removed in a water-jet-pump vacuum. The residue was dissolved in benzene and twice chromatographed on 40 g of neutral alumina (Brockmann grade II). Then the solvent was removed.

2,4,6-Tris(*N*-diisopropoxythiophosphorylbenzimidoyl)-1,3,5-triazine Xa. Yield 5.54 g (57.4%), n_D^{20} 1.5970, δ_P 56 ppm. Found, %: C 49.21; H 5.59; P 8.91. $C_{42}H_{57}N_6O_6P_3S_6$. Calculated, %: C 49.12; H 5.55; P 9.06.

2,4,6-Tris(*S*-isothiobenzamido-*N*-diisopropoxyphosphoryl)-1,3,5-triazine Xb. Yield 4.80 g (49%), n_D^{20} 1.6428, δ_P –3 ppm. Found, %: C 55.05; H 5.60; P 9.39. $C_{42}H_{57}N_6O_9P_3S_3$. Calculated, %: C 55.20; H 5.82; P 9.49.

ACKNOWLEDGMENTS

The study was financially supported by the Russian Foundation for Basic Research (project no. 00-03-32 742) and the joint program of CRDF and the Ministry of Education of the Russian Federation “Basic Research and Higher Education” (grant no. REC-007).

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