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Reaction of Diethyl Esters of 1-Acylamino-2,2-dichlorovinylphosphonic Acids and Their Analogs with the Lawesson's Reagent

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Abstract—Diethyl esters of 1-acylamino-2,2-dichlorovinylphosphonic acids and their analogs upon heating with the Lawesson's reagent are converted into the earlier unknown substituted 1,3-thiazol-4-ylthiophosphonates in high yields.

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Earlier the reactions of diethyl esters of 1-acylamino-2,2-dichlorovinylphosphonic acids **I** prepared from tetrachloroethylamides of carboxylic acids and triethylphosphite [1] with amines, hydrazines, sodium hydrogen sulfide have been studied. As a rule they lead to 4-phosphorylated derivatives of 5-amino- and 5-mercapto-1,3-oxazoles [2–6].

In this work the reaction of compounds **I** and their analogs **II** with the Lawesson's reagent was first studied and shown to lead to the earlier unknown diethyl esters of 2-aryl-5-chloro-1,3-thiazol-4-ylthiophosphonic acids (see the sequences of transformations **I** → **III** → **V** → **VII** and **II** → **IV** → **VI** → **VIII**, respectively, on the scheme) (Table 1).

Table 1. Yields, constants, and elemental analysis of compounds **I, II, VII–IX**

Comp. no.	Yield, %	mp, °C (solvent)	Found, %				Formula	Calculated, %			
			Cl	N	P	S		Cl	N	P	S
Id	84	174–176 (EtOH)	17.49	7.75	7.11	–	$C_{13}H_{15}Cl_2N_2O_6P$	17.85	7.05	7.80	–
IIa	71	97–99 (ethyl acetate)	8.21	3.56	7.49	7.18	$C_{20}H_{23}ClNO_4PS$	8.06	3.18	7.04	7.29
IIb	78	107–109 (ethyl acetate)	15.28	2.89	7.05	6.63	$C_{19}H_{20}Cl_2NO_4PS$	15.40	3.04	6.73	6.97
IIc	80	115–117 (ethyl acetate)	14.86	2.66	6.29	6.82	$C_{20}H_{22}Cl_2NO_4PS$	14.95	2.95	6.53	6.76
IId	82	144–146 (ethyl acetate)	21.72	3.12	6.92	6.83	$C_{19}H_{19}Cl_3NO_4PS$	21.50	2.83	6.26	6.48
IIe	77	182–184 (ethyl acetate)	7.42	5.28	6.09	6.31	$C_{20}H_{22}ClN_2O_6PS$	7.31	5.78	6.39	6.61
IIf	82	160–162 (ethyl acetate)	13.91	5.04	6.43	6.27	$C_{19}H_{19}Cl_2N_2O_6PS$	14.03	5.54	6.13	6.35
VIIa	58	73–75 (EtOH)	10.09	3.83	8.74	18.62	$C_{13}H_{15}ClNO_2PS_2$	10.19	4.03	8.91	18.44
VIIb	61	79–81 (EtOH)	9.91	4.02	8.91	17.56	$C_{14}H_{17}ClNO_2PS_2$	9.80	3.87	8.56	17.72
VIIc	65	103–105 (EtOH)	18.25	3.98	8.53	16.91	$C_{13}H_{14}Cl_2NO_2PS_2$	18.55	3.66	8.10	16.78
VIId	67	95–97 (EtOH)	8.88	7.84	8.02	16.12	$C_{13}H_{14}ClN_2O_4PS_2$	9.03	7.13	7.88	16.32
VIIIa	51	88–90 (C_6H_6)	14.87	3.14	6.12	19.08	$C_{19}H_{18}Cl_2NO_2PS_3$	14.46	2.86	6.32	19.61
VIIIb	53	93–95 (C_6H_6)	–	5.03	5.95	20.44	$C_{20}H_{21}N_2O_4PS_3$	–	5.83	6.45	20.02

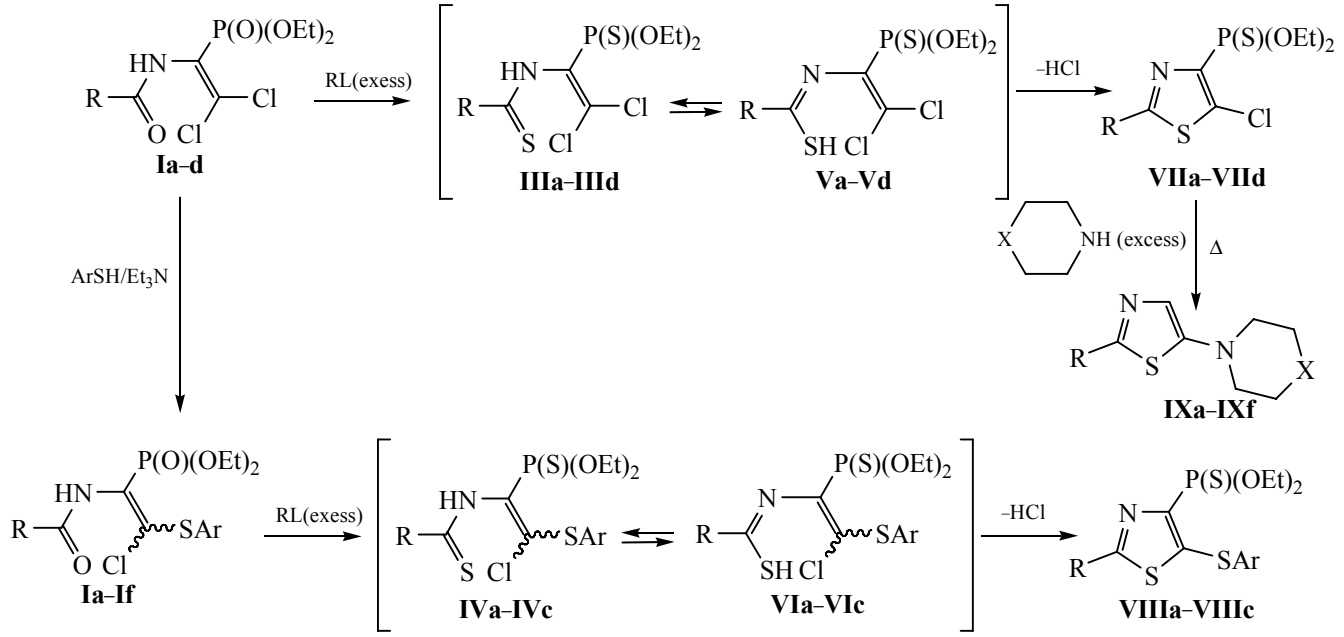
Table 1. (Contd.)

Comp. no.	Yield, %	mp, °C (solvent)	Found, %				Formula	Calculated, %			
			Cl	N	P	S		Cl	N	P	S
VIIIc	57	97–99 (C_6H_6)	6.98	5.91	6.86	19.06	$C_{19}H_{18}ClN_2O_4PS_3$	7.08	5.59	6.18	19.20
IXa	41	80–83[a] (EtOH)	–	12.08	–	13.44	$C_{14}H_{16}N_2S$	–	11.46	–	13.12
IXb	47	131–133 (EtOH)	–	11.91	–	13.36	$C_{13}H_{14}N_2OS$	–	11.37	–	13.02
IXc	43	108–110 (EtOH)	–	11.17	–	12.21	$C_{15}H_{18}N_2S$	–	10.84	–	12.41
IXd	49	110–112 (EtOH)	–	10.26	–	12.72	$C_{14}H_{16}N_2OS$	–	10.76	–	12.32
IXe	54	144–146 (EtOH)	12.92	10.11	–	11.13	$C_{13}H_{13}ClN_2OS$	12.63	9.98	–	11.42
IXf	57	151–153 (EtOH)	–	14.82	–	11.22	$C_{13}H_{13}N_3O_3S$	–	14.42	–	11.01

[a] Melting point corresponds to the literature data [8].

The Lawesson's reagent produced complex action on compounds **I** and **II** since not only thionation of the carbonyl and the phosphoryl groups occurs with the formation of the intermediate products **III** and **IV** or their prototropic tautomers **V** and **VI** but also their subsequent cyclocondensation with the participation of the dichlorovinyl or chlorovinyl fragments.

The structure of compounds **VII** and **VIII** is consistent with the data of the IR and ^{1}H NMR spectra, which prove that the reaction of substrates **I** and **II** with the Lawesson's reagent proceeds with the participation of the acylamine moieties (Table 2). Thus, in the IR spectra of compounds **VII** and **VIII** the absorption bands at 1600–1700 and 3050–3500 cm^{-1}, which are characteristic of the starting compounds, are



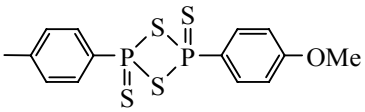
I, VII: R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 3-$O_2NC_6H_4$ (**d**); **II**: R = Ph, Ar = 4-MeC_6H_4 (**a**), 4-ClC_6H_4 (**b**); R = 4-MeC_6H_4, Ar = 4-ClC_6H_4 (**c**); R = 4-ClC_6H_4, Ar = 4-ClC_6H_4 (**d**); R = 3-$O_2NC_6H_4$, Ar = 4-MeC_6H_4 (**e**), 4-ClC_6H_4 (**f**); **VIII**: R = Ar = 4-ClC_6H_4 (**a**); R = 3-$O_2NC_6H_4$, Ar = 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**); **IX**: R = Ph; X = CH_2 (**a**), O (**b**); R = 4-MeC_6H_4, X = CH_2 (**c**), O (**d**); R = 4-ClC_6H_4, X = CH_2 (**e**); RL = 

Table 2. Spectral data of compounds **I, II, VII–IX**

Comp. no.	^{1}H NMR spectrum, δ, ppm (ДМСО-d_6)	^{31}P NMR spectrum, δ, ppm (DMSO-d_6)	IR spectrum (KBr), ν, cm^{-1}
Id	1.20 m (6H, 2CH_3), 4.09 m (4H, 2CH_2), 7.73–8.51 m (4H_{arom}), 10.33 s (1H, NH)	–	1246 (P=O), 1673 (C=O), 3085–3205 (NH_{ass})
IIb	1.23 m (6H, 2CH_3), 4.10 m (4H, 2CH_2), 7.48–7.97 m (9H_{arom}), 10.04 s, 10.15 s (1H, NH)	9.10, 10.00 (1:1)[a]	1232 (P=O), 1667[b] (C=O), 3080–3205 (NH_{ass})
IId	1.21 m (6H, 2CH_3), 4.12 m (4H, 2CH_2), 7.51–7.96 m (8H_{arom}), 10.18 s, 10.21 s (1H, NH)	8.82, 9.90 (1:3)[a]	1242 (P=O), 1662[b] (C=O), 3050–3200 (NH_{ass})
VIIb[c]	1.34 t (6H, 2CH_3), 2.36 s (3H, CH_3), 4.26 m (4H, 2CH_2), 7.35–7.77 m (4H_{arom})	69.90	1620–1700, 3050–3500 (no bands)
VIIc	1.34 t (6H, 2CH_3), 4.25 m (4H, 2CH_2), 7.63–7.90 m (4H_{arom})	69.70	1600–1700, 3050–3500 (no bands)
VIId	1.35 t (6H, 2CH_3), 4.27 m (4H, 2CH_2), 7.81–8.62 m (4H_{arom})	66.80	1600–1700, 3050–3500 (no bands)
VIIIb[d]	1.35 t (6H, 2CH_3), 2.36 s (3H, CH_3), 4.27 m (4H, 2CH_2), 7.32–8.52 m (8H_{arom})	71.00	1600–1700, 3050–3500 (no bands)
IXb	3.14–3.75 m (8H, 4CH_2), 7.13 s (1H, C^4–H thiazole), 7.33–7.75 m (5H_{arom})	–	1600–1700, 3050–3500 (no bands)
IXc	1.58–3.12 m (10H, 5CH_2), 2.34 s (3H, CH_3), 6.91 s (1H, C^4–H thiazole), 7.20–7.58 m (4H_{arom})	–	1600–1700, 3050–3500 (no bands)
IXd	2.34 s (3H, CH_3), 3.10–3.75 m (8H, 4CH_2), 7.00 s (1H, C^4–H thiazole), 7.21–7.60 m (4H_{arom})	–	1600–1700, 3050–3500 (no bands)
IXe	3.13–3.76 m (8H, 4CH_2), 7.06 s (1H, C^4–H thiazole), 7.43–7.72 m (4H_{arom})	–	1600–1700, 3050–3500 (no bands)
IXf	3.18–3.76 m (8H, 4CH_2), 7.17 s (1H, C^4–H thiazole), 7.72–8.49 m (4H_{arom})	–	1600–1700, 3050–3500 (no bands)

[a] Integral intensities are given in parentheses. [b] Band with a shoulder. [c] Mass spectrum: *m/z* 362 (M^+). [d] Mass spectrum: *m/z* 481 (M^+).

absent. At the same time, mass spectra and elemental analysis confirm the presence of two (compounds **VII**) or three (compounds **VIII**) sulfur atoms. The presence of the thiophosphoryl group in these products is proved by the signals in the ^{31}P NMR spectra at 69–71 ppm characteristic of the P=S bond [7].

It should be noted that the mobility of the chlorine atoms in compounds **VII** is low, therefore it is not replaced by the action of thiols or amines at long heating in ethanol. However, when refluxed in piperidine or morpholine without solvent, compounds **VII** suffer replacement of chlorine by the residue of the nitrogen base, and, moreover, the carbon-phosphorus bond is ruptured so that the derivatives of 5-aminothiazole without substituents in the 4 position of the ring are formed.

The structure of compounds **IX** is confirmed by their ^{1}H NMR spectra, where characteristic signals of the piperidine and the morpholine protons are observed at δ 1.58–3.76 ppm, as well as singlet signals at δ 6.91–7.17 ppm, which belong to the H^4 proton of the thiazole ring. Besides, one of these compounds **IXa** was earlier prepared by alternative protocol [8] that unequivocally proves the structure of compounds **IX** as well as their precursors **VII** and analogs **VIII**.

EXPERIMENTAL

IR spectra were recorded on a Vertex 70 spectrometer in KBr, ^{1}H and ^{31}P NMR spectra were registered on a Varian VXR-300 spectrometer at 300 and 81 MHz, respectively, in DMSO-d_6, with TMS as an internal standard. Mass spectra were taken on an Agilent 1100/DAD/MSD VL G1965 instrument. Melting points were measured on a Fisher-Johns unit.

Diethyl esters of 1-acylamino-2,2-dichlorovinylphosphonic acids (Ia–Ic) were prepared as described in [1].

Diethyl ester of 1-(3-nitrobenzoylamino-2,2-dichlorovinylphosphonic acid (Id) was synthesized by the scheme used for compounds **Ia–Ic** [1].

Diethyl esters of 2-arylthio-1-acylamino-2,2-dichlorovinylphosphonic acids (IIa–IIf). To the solution of 0.01 mol of compound **Ia–Id** in 30 ml of acetonitrile 0.01 mol of 4-methylthiophenol or 4-chlorothiophenol and equimolar amount of triethylamine were added, and the mixture was left overnight at room temperature. Triethylamine hydrochloride was filtered off, the solvent was removed in a vacuum, the residue was treated with water, the precipitate was filtered off, and compounds **IIa–IIf** were purified by crystallization.

Diethyl esters of (2-aryl-5-chloro-1,3-thiazol-4-yl)thiophosphonic acids (VIIa–VIId). To the solution of 0.01 mol of compound **Ia–Id** in 50 ml of dry dioxane 0.02 mol of the Lawesson's reagent was added, the mixture was refluxed for 6 h, the solvent was removed in a vacuum, the residue was treated with water, then with 20% aqueous sodium hydroxide to remove the unreacted Lawesson's reagent. The precipitate was filtered off and compounds **VIIa–VIId** were purified by crystallization.

Diethyl esters of (2-aryl-5-arylthio-1,3-thiazol-4-yl)thiophosphonic acids (VIIIa–VIIIc) were prepared similarly to thiazoles **VIIa–VIId** from compounds **IId–IIf**.

2-Aryl-5-piperidino(morpholino)-1,3-thiazoles (IXa–IXf). To 0.01 mol of compound **VIIa–VIId** 20 ml of piperidine or morpholine was added, the mixture was refluxed for 4 h, the excess of piperidine or morpholine was removed in a vacuum, the residue was treated with water, the precipitate was filtered off, and compounds **IXa–IXf** were purified by crystallization.

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