Russian Journal of General Chemistry, Vol. 71, No. 11, 2001, pp. 1726–1728. Translated from Zhurnal Obshchei Khimii, Vol. 71, No. 11, 2001, pp. 1822–1824.

Synthesis and Transformations of 4-Phosphorylated 2-Alkyl(aryl)-5-hydrazinooxazoles

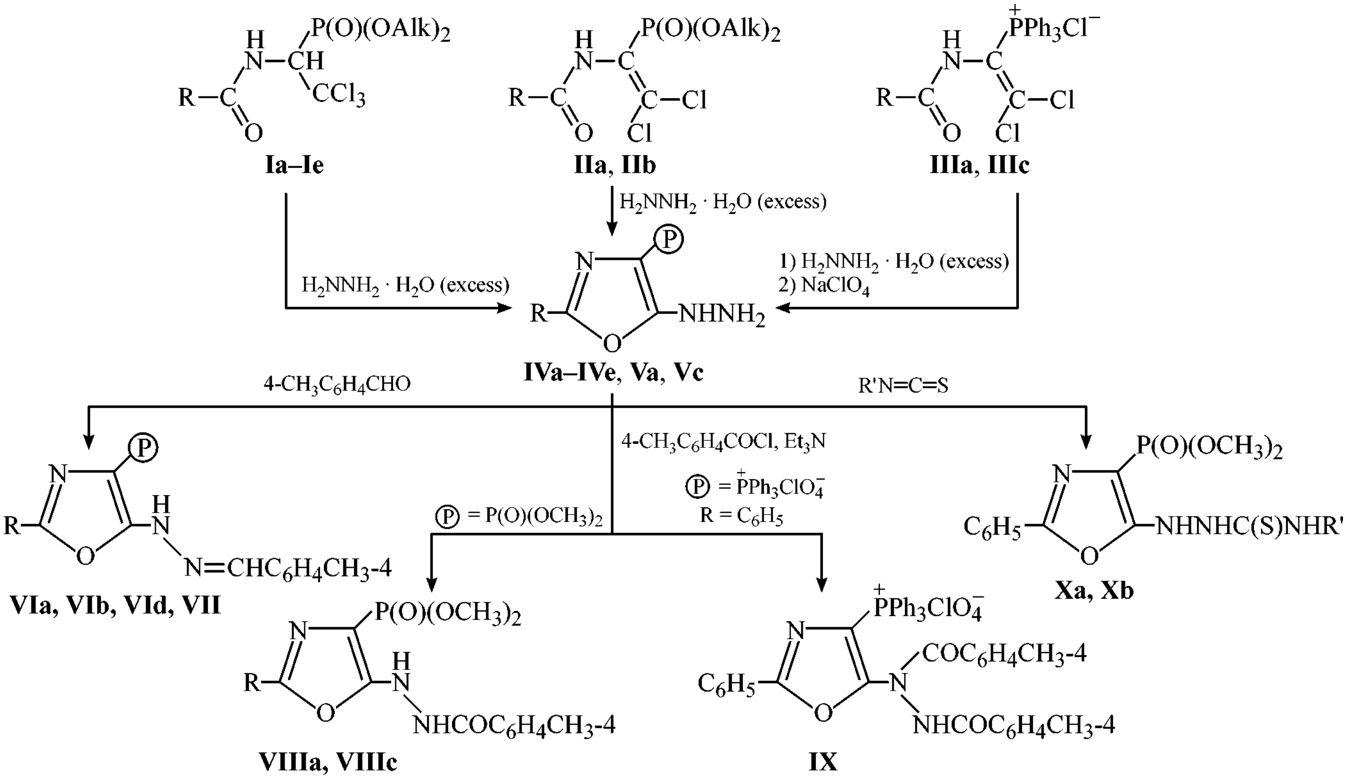
V. S. Brovarets, R. N. Vydzhak, S. G. Pil'o, K. V. Zyuz', and B. S. Drach

Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine, Kiev, Ukraine

Received August 4, 2000

Abstract—Treatment of 1-phosphorylated 2,2-dichloroethenylcarboxamides with excess hydrazine hydrate gives in high yields phosphorylated derivatives of 2-alkyl(aryl)-5-hydrazinooxazoles containing the $P(O)(OCH_3)_2$, $P(O)(OC_2H_5)_2$, and $P^+(C_6H_5)_3ClO_4^-$ groups in the 4-position of the ring. The presence of the hydrazine group in these oxazole derivatives was confirmed not only by the spectral data, but also by the reactions with *p*-toluic aldehyde, *p*-toluic chloride, and phenyl isothiocyanate.

Reaction of three types of phosphorus-containing electrophilic reagents **I**–**III** with amines is thoroughly studied [1–3]. In this work we found that compounds **I**–**III** readily react not only with amines, but also with hydrazine hydrate. The reaction yields phosphorus-containing 5-hydrazinooxazoles **IV** and **V** whose structure was confirmed by the IR and ^{1}H NMR spectra (see Experimental; Table 1). For example, comparison of the IR spectra of the initial compounds **I**–**III** and the products of their reaction with hydrazine hydrate **IV** and **V** suggests disappearance of the carbonyl group of the amide moiety which takes part in cyclization. At the same time, the ^{1}H NMR spectra of **IV** and **V** contain a broad singlet of two protons of the NNH_2 group in the range 4.2–4.8 ppm.



R = C_6H_5 (**Ia–VIa, Ib, IIb, VIb, VII, VIIIa**), 4-ClC_6H_4 (**Ic, IIIc–Vc, VIIIc**), CH_3 (**Id, IVd, VId**), $C_6H_5CH=CH$ (**Ie, IVe**); Alk = CH_3 (**Ia, Ic, Id, IIa**), C_2H_5 (**Ib, IIb**); R' = C_6H_5 (**Xa**), $CH_2=CHCH_2$ (**Xb**); Ⓟ = $P(O)(OCH_3)_2$ (**IVa, IVc, IVd, VIa, VId**), $P(O)(OC_2H_5)_2$ (**IVb, VIb**), $\overset{+}{P}Ph_3ClO_4^-$ (**Va, Vc, VII**).

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Table 1. ^{1}H NMR spectra of **IV**–**IX**

Comp. no.	δ, ppm (DMSO-d_6)
IVa	3.69 d (6H, $2CH_3O$, $^3J_{HP}$ 12.1 Hz), 4.80 br.s (2H, NH_2), 7.48–7.84 m (6H, C_6H_5, NH)
IVe	3.67 d (6H, $2CH_3O$, $^3J_{HP}$ 12.0 Hz), 4.75 br.s (2H, NH_2), 7.03–7.64 m (8H, C_6H_5, CH=CH, NH)
Va	4.20 br.s (2H, NH_2), 7.48–7.95 m (21H, $4C_6H_5$, NH), 9.82 br.s (1H, NH)
VIa	2.35 s (3H, CH_3), 3.74 d (6H, $2CH_3O$, $^3J_{HP}$ 11.9 Hz), 7.25–7.80 m (9H, C_6H_5, C_6H_4), 8.35 s (1H, CH=N), 10.86 s (1H, NH)
VIb	1.27 t (6H, $2CH_3$), 2.35 s (3H, CH_3), 4.07 q (4H, $2CH_2O$), 7.28–7.95 m (9H, C_6H_5, C_6H_4), 8.29 s (1H, CH=N), 10.75 s (1H, NH)
VId	2.38 d (6H, $2CH_3O$, $^3J_{HP}$ 12.5 Hz), 3.63 s (3H, CH_3), 3.70 s (3H, CH_3), 7.23–7.53 m (4H, C_6H_4), 8.18 s (1H, CH=N), 10.35 s (1H, NH)
VII	2.21 s (3H, CH_3), 6.46–7.95 m (25H, $4C_6H_5$, C_6H_4, CH=N), 12.79 br.s (1H, NH)
VIIIa	2.38 s (3H, CH_3), 3.73 d (6H, $2CH_3O$, $^3J_{HP}$ 11.6 Hz), 7.35–7.88 m (9H, C_6H_5, C_6H_4), 8.65 br.s (1H, NH), 10.71 br.s (1H, NH)
VIIIc	2.38 s (3H, CH_3), 3.67 d (6H, $2CH_3O$, $^3J_{HP}$ 11.9 Hz), 7.40–7.84 m (8H, $2C_6H_4$), 8.77 s (1H, NH), 10.75 s (1H, NH)
IX	2.26 s (3H, CH_3), 2.36 s (3H, CH_3), 7.13–7.88 m (28H, $4C_6H_5$, $2C_6H_4$), 11.95 br.s (1H, NH)

Table 2. Constants, yields, and elemental analyses of **IV**–**X**

Comp. no.	Yield, %	mp, °C (solvent for crystallization)	Found, %			Formula	Calculated, %		
			Cl (S)	N	P		Cl (S)	N	P
IVa	84[a]	104–105 (benzene)	–	14.67	10.81	$C_{11}H_{14}N_3O_4P$	–	14.84	10.94
IVb	77[a]	–[b]	–	13.39	9.81	$C_{13}H_{18}N_3O_4P$	–	13.50	9.95
IVc	86	48–50 (aqueous methanol)	10.96	13.15	9.60	$C_{11}H_{13}ClN_3O_4P$	11.16	13.23	9.75
IVd	72	–[b]	–	18.88	13.86	$C_6H_{12}N_3O_4P$	–	19.00	14.01
IVe	75	118–120 (benzene)	–	13.58	9.90	$C_{13}H_{16}N_3O_4P$	–	13.59	10.02
Va	78	206–209[c] (methanol)	6.49	7.83	5.67	$C_{27}H_{23}ClN_3O_5P$	6.62	7.84	5.78
Vc	82	208–210[c] (methanol)	12.65	7.15	5.35	$C_{27}H_{22}Cl_2N_3O_5P$	12.43	7.37	5.43
VIa	79	118–120 (ethanol)	–	10.71	7.92	$C_{19}H_{20}N_3O_4P$	–	10.90	8.04
VIb	83	136–137 (ethanol)	–	10.15	7.40	$C_{21}H_{24}N_3O_4P$	–	10.16	7.49
VId	72	120–121 (aqueous ethanol)	–	12.90	9.43	$C_{14}H_{18}N_3O_4P$	–	13.00	9.58
VII	85	230–232[c] (ethanol)	5.39	6.45	4.79	$C_{35}H_{29}ClN_3O_5P$	5.56	6.59	4.85
VIIIa	82	155–158 (methanol)	–	9.65	7.05	$C_{19}H_{20}N_3O_5P$	–	9.72	7.16
VIIIc	74	152–155 (acetonitrile)	7.63	8.91	6.52	$C_{19}H_{19}ClN_3O_5P$	7.60	9.00	6.64
IX	68	238–242[c] (acetonitrile)	4.45	5.32	3.93	$C_{43}H_{35}ClN_3O_7P$	4.59	5.44	4.01
Xa	77	145–147 (aqueous ethanol)	(7.53)	13.28	7.39	$C_{18}H_{19}N_4O_4PS$	(7.66)	13.39	7.40
Xb	69	75–80 (aqueous ethanol)	(8.25)	14.51	7.90	$C_{15}H_{19}N_4O_4PS$	(8.39)	14.65	8.10

[a] Yield in procedure *a*. [b] The product was isolated as a viscous oil. [c] Melts with noticeable decomposition.

Also, similarly to other alkyl, aryl, and heterylhydrazines, compounds **IV** and **V** readily react with aldehydes, acid chlorides, and aryl isothiocyanates (see the transformations **IV** → **VI**, **V** → **VII**, **IV** → **VIII**, and **V** → **IX** or **X** in the scheme).

It is quite evident that from the two new types of phosphorylated heterylhydrazines **IV** and **V** it is possible to obtain not only compounds **VI**–**X**, but also numerous other derivatives, because compounds **I**–**III** are readily available, and their cyclocondensation with hydrazine hydrate proceeds quite selectively.

The yields and physicochemical characteristics of the obtained products are listed in Table 2.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer in KBr pellets. The ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer in DMSO-d_6 relative to TMS.

2-Alkyl(aryl)-5-hydrazino-4-dialkoxyphosphoryloxazoles IVa–IVe. *a*. To a solution of **Ia**–**Ie** in 15 ml of THF was added 0.045 mol of hydrazine hydrate. The resulting mixture was stirred for 72 h at 20–25°C, the solvent was removed in a vacuum, and the residue was treated with water. Compounds **IVa**, **IVc**, and **IVe** were purified by crystallization. Compounds **IVb** and **IVd** were extracted from the aqueous emulsion with methylene chloride and dried over sodium sulfate, the solvent was removed in a vacuum, and the resulting viscous oil was used in further reactions without additional purification. The IR spectra of **IVa**–**IVe** contain no intense bands in the range 1620–1750 cm^{-1}.

b. To a solution of **IIa** or **IIb** in 15 ml of THF was added 0.035 mol of hydrazine hydrate, and compound **IVa** or **IVb** was isolated as described above in a 70–80% yield. The mixed sample of two preparations of **IVa** obtained by procedures *a* and *b* gave no depression of the melting point.

(2-Aryl-5-hydrazinooxazol-4-yl)triphenylphosphonium perchlorates Va and Vc. To a solution of 0.02 mol of phosphonium salt **IIIa** or **IIIc** in 25 ml of methanol was added 0.03 mol of hydrazine hydrate. The resulting mixture was left for 12 h at 20–25°C, the precipitate was filtered off, and 0.5 ml of acetic acid and 5 ml of saturated aqueous solution of sodium perchlorate were added. The precipitate was filtered off, and compound **Va** or **Vc** was purified by crystallization.

***p*-Toluic aldehyde 2-[4-dialkoxyphosphoryl-2-methyl(phenyl)oxazol-4-yl]hydrazones VIa, VIb, and VId.** A mixture of 0.001 mol of compound **IVa**, **IVb**, or **IVd**, 0.001 mol of *p*-toluic aldehyde, and 10 ml of ethanol was refluxed for 3 h, the solvent was removed in a vacuum, and compound **VIa**, **VIb**, or **VId** was purified by crystallization.

***p*-Toluic aldehyde 2-[4-triphenylphosphonio-2-phenyloxazol-4-yl]hydrazone perchlorate (VII).** To a solution of 0.001 mol of phosphonium salt **Va** in 10 ml of ethanol was added 0.001 mol of *p*-toluic aldehyde. The resulting mixture was refluxed for 3 h, the precipitate was filtered off, and compound **VII** was purified by crystallization. IR spectrum, ν, cm^{-1}: 1640 (C=N), 3200 (NH$_{\text{assoc}}$).

2-Aryl-4-dimethoxyphosphoryl-5-(2-*p*-toluylhydrazino)oxazoles VIIIa and VIIIc. To a solution of 0.005 mol of **IVa** or **IVc** in 15 ml of anhydrous acetonitrile were added 0.005 mol of triethylamine and 0.005 mol of *p*-toluyl chloride. The mixture was left for 48 h at 20–25°C, and the precipitate was filtered off and washed with water. Compound **VIIIa** or **VIIIc** was purified by crystallization. IR spectrum of **VIIIa**, ν, cm^{-1}: 1680 (C=O), 3250 (NH$_{\text{assoc}}$).

5-[(1,2-Di-*p*-toluyl)hydrazino]-4-triphenylphosphonio-2-phenyloxazole perchlorate IX. To a suspension of 0.002 mol of phosphonium salt **Va** in 10 ml of anhydrous acetonitrile, 0.0042 mol of triethylamine and then 0.004 mol of *p*-toluyl chloride were added at cooling with ice-cold water. The mixture was left for 1 h at 20–25°C, 5 ml of diethyl ether was added, the precipitate was filtered off and washed with water, and phosphonium salt **IX** was purified by crystallization. IR spectrum, ν, cm^{-1}: 1690 (C=O), 1720 (C=O), 3300 (NH$_{\text{assoc}}$).

4-Dimethoxyphosphoryl-2-phenyl-5-(4-phenylthiosemicarbazido)oxazole Xa. To a solution of 0.003 mol of **IVa** in 10 ml of acetonitrile was added 0.0036 mol of phenyl isothiocyanate. The mixture was refluxed for 3 h, the precipitate was filtered off, and compound **Xa** was purified by crystallization.

5-(4-Allylthiosemicarbazido)-4-dimethoxyphosphoryl-2-phenyloxazole Xb was obtained similarly to **Xa** from substituted 5-hydrazinooxazole **IVa** and allyl isothiocyanate.

ACKNOWLEDGMENTS

The authors are grateful to the State Foundation for Basic Research of Ukraine (project no 3.4/26) for the financial support.

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