

LETTERS  
TO THE EDITOR

## Unusual Phosphorylation of 2-Amino-4-phenylthiazole with Phosphorous Acid Ester Amides

L. K. Sal'keeva<sup>a</sup>, P. Voitichek<sup>b</sup>, E. K. Taishibekova<sup>a</sup>, A. A. Zhortarova<sup>a</sup>,  
A. K. Shibaeva<sup>a</sup>, L. M. Sugralina<sup>a</sup>, A. A. Muratbekova<sup>a</sup>, A. K. Sal'keeva<sup>c</sup>

<sup>a</sup> Buketov Karaganda State University, ul. Universititskaya 28, Karaganda, 100028 Kazakhstan  
e-mail: LSalkeeva@mail.ru

<sup>b</sup> Charles University, Prague, Czech Republic

<sup>c</sup> Karaganda State Technical University, Karaganda, Kazakhstan

Received July 28, 2014

**Keywords:** aminothiazoles, phosphorylation, phosphorous acid ester amides, diphosphetidine

**DOI:** 10.1134/S1070363214120275

Phosphorylated thiazoles present significant theoretical and practical interest being still poorly investigated class of compounds. Several attempts were performed to synthesize phosphorus-containing derivatives of thiazole and its homologs [1–3]. Particularly, direct condensation of 2-aminothiazole with aromatic aldehydes and dialkyl phosphites in the presence of alkali metal alcoholates was unsuccessful probably due to low basicity of 2-aminothiazole ( $pK_a$  5.39) [4]. Phosphonomethylation of 2-aminothiazole succeeded by the reaction of dialkyl phosphites with benzaldehyde diacetal in the presence of boron trifluoride etherate [5].

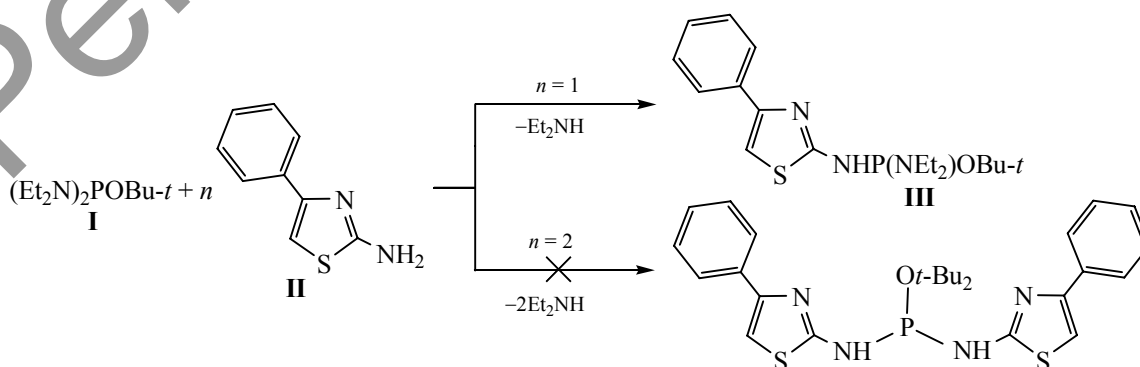
Earlier a possibility of 2-amino-4-phenylthiazole phosphorylation by the reaction of transamidation with tetraethyldiamido-*tert*-butyl phosphite **I** was disco-

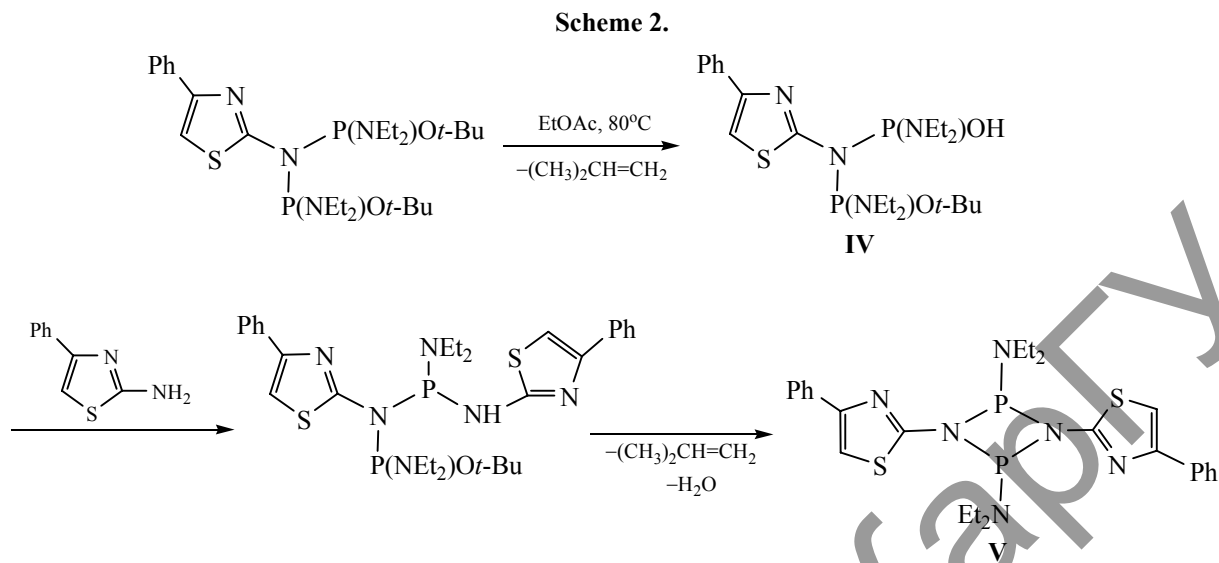
vered [6]. Conditions of the phosphorylation were found and some reaction regularities were studied. Particularly, phosphorylation was found to be proceeded at the reagents ratio of 1 : 1. Furthermore, chemical modification of the synthesized *tert*-butyl-*N*-thiazolyl amido phosphite **III** in reactions with various electrophilic reagents was studied [7] (Scheme 1).

It seemed interesting to investigate reaction of phosphite **I** with 2-amino-4-phenylthiazole **II** in a ratio of 2 : 1 with the aim of adding two phosphorus(III) atoms to the nitrogen atom of thiazole that would substantially widen possibility for chemical modification of the obtained compound.

Thus, the reaction of phosphite **I** with 2-amino-4-phenylthiazole **II** in a ratio of 2 : 1 in ethyl acetate at heating and continuous distilling off diethylamine led

Scheme 1.





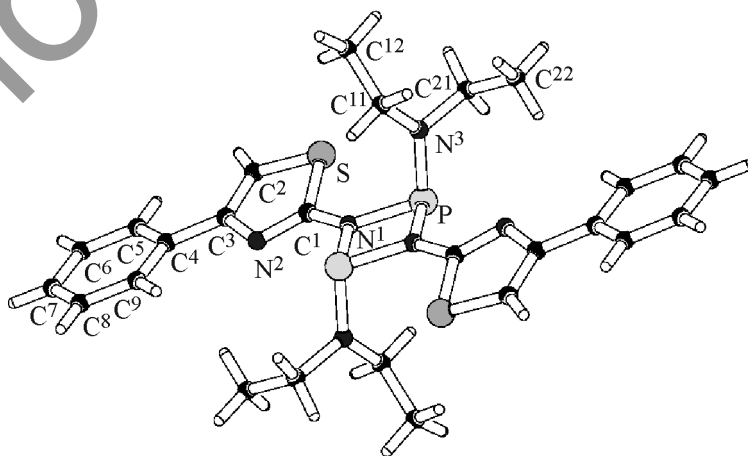
to the formation of viscous oily compound which completely crystallized at standing providing white crystals with mp 162°C. According to the X-ray analysis (see figure), the structure of the synthesized compound corresponded to the four-membered phosphetane 1,3-bis(4-phenylthiazol-2-yl)-2,4-bis(*N,N*-diethylamino)-1,3-diazo-2,4-diphosphetidine.

Most probably, the phosphorylation proceeded through complete transamidation with two moles of amidophosphite **I**. The formed bis-phosphorylated aminothiazole under the reaction conditions underwent isomerization with elimination of *tert*-butyl cation due to steric hindrances which furthermore formed isobutylene identified in the reaction mixture by means

of mass-spectroscopy. The formed product **IV** was ready to the following transamidation and the closure of the four-membered cycle **V** with water molecule elimination (Scheme 2).

**1,3-Bis(4-phenylthiazol-2-yl)-2,4-bis(*N,N*-diethylamino)-1,3-diazo-2,4-diphosphetidine (V).** Yield 82%, mp 162°C. <sup>1</sup>H NMR spectrum (DMSO-*d*<sub>6</sub>), δ, ppm: 5.52 s (2H, H<sup>5</sup>, thiazole), 6.70–8.26 m (10H, C<sub>6</sub>H<sub>5</sub>), 1.12 s (6H, CH<sub>3</sub>), 2.87–3.42 m (4H, CH<sub>2</sub>). Mass-spectrum: *m/z* 554. Found, %: C 56.52; H 5.95; N 15.38; P 11.34; S 11.31. C<sub>26</sub>H<sub>32</sub>N<sub>6</sub>P<sub>2</sub>S<sub>2</sub>. Calculated, %: C 56.32; H 5.78; N 15.16; P 11.19; S 11.55.

The NMR spectrum was recorded on a Bruker DRX-300 (300 MHz) and Jeol ECX-400 (400 MHz)



General view of the molecule of 1,3-bis(4-phenylthiazol-2-yl)-2,4-bis(*N,N*-diethylamino)-1,3-diazo-2,4-diphosphetidine **V**.

spectrometers. Mass spectrum was registered on a Varian Saturn 2000K instrument. X-Ray analysis was performed on a D/MAX-RAPID II diffractometer.

## REFERENCES

1. Prokof'eva, A.F. and Aleshnikova, T.V., *Zh. Obshch. Khim*, 1984, vol. 54, no. 3, p. 525.
2. Ivancsics, C. and Zbiral, E., *Monatsh. Chem.*, 1975, vol. 106, p. 839. DOI: 10.1007/BF00900862.
3. Lobanov, O.P., Martynyuk, A.P., and Drach, B.S., *Zh. Obshch. Khim*, 1980, vol. 50, no. 10, p. 2248.
4. Albert, A., Goldacre, R.J., and Phillips, J., *J. Chem. Soc.*, 1948, p. 2240.
5. Lugovkin, B.P., *Zh. Obshch. Khim*, 1974, vol. 44, no. 1, p. 106.
6. Sal'keeva, L.K., Nurmaganbetova, M.T., and Minaeva, E.V., *Russ. J. Gen. Chem.*, 2005, vol. 75, no. 12, p. 1975. DOI: 10.1134/S1070363206090076.
7. Sal'keeva, L.K., Nurmaganbetova, M.T., and Minaeva, E.V., *Russ. J. Gen. Chem.*, 2006, vol. 76, no. 9, p. 1397. DOI: 10.1134/S1070363206090076.