Impact Factor:					
	ISRA (India) = 6.317	SIS (USA) = 0.912	ICV (Poland) = 6.630
	ISI (Dubai, UAE) = 1.582	РИНЦ (Russia) = 3.939	PIF (India) = 1.940
	GIF (Australia) = 0.564	ESJI (KZ) = 8.771	IBI (India) = 4.260
	JIF = 1.500	SJIF (Morocco) = 7.184	OAJI (USA) = 0.350

SOI: 1.1/TAS DOI: 10.15863/TAS

International Scientific Journal

Theoretical & Applied Science

p-ISSN: 2308-4944 (print) **e-ISSN:** 2409-0085 (online)

Year: 2023 **Issue:** 01 **Volume:** 117

Published: 22.01.2023 **http://T-Science.org**

Issue Article

A.M. Maharramov
Baku State University
Academician

Kh.A. Asadov
Baku State University
researcher

E.Z. Huseyinov
Baku State University
researcher
elnur.huseynov85@gmail.com

F. M. Abdullaeva
Institute of Petrochemical Processes named after Yu. G. Mamedaliev
researcher

S. B. Asadova
Institute of Petrochemical Processes named after Yu. G. Mamedaliev
researcher

SYNTHESIS OF PHOSPHORYLATED 1,3,4-THIADIAZINE BASED ON THE REACTION OF PHOSPHORYLATED CHLORALDEHYDE WITH 4-AMINO-1,2,4-TRIAZOLE-3-THIONE

Abstract: *Has been investigated the behavior of phosphoryl-α-chloroaldehydes under the conditions of the Bose reaction with the cyclic analogue of thiosemicarbazide-4-amino-1,2,4-triazole-3-thione, leading to the synthesis of the triazolo [3,4b]-1,3,4-thiadiazine derivative which is possessing antibacterial, antifungal and other types of biological activity.*

Key words: *chloraldehyd, thiadiazin, triazol, thiosemicarbazide, biological activity.*

Language: *English*

Citation: Maharramov, A. M., et al. (2023). Synthesis of phosphorylated 1,3,4-thiadiazine based on the reaction of phosphorylated chloraldehyde with 4-amino-1,2,4-triazole-3-thione. *ISJ Theoretical & Applied Science, 01 (117),* 472-475.

Soi: http://s-o-i.org/1.1/TAS-01-117-35 ***Doi***: https://dx.doi.org/10.15863/TAS.2023.01.117.35

Scopus ASCC: *1600.*

Introduction

The most common among thiadiazines are 1,3,4-thiadiazines, the methods of synthesis of which consist mainly in the reactions of compounds that are synthetic equivalents of the C^+-C^+ + and S^--C-N-N^- synthons. This is primarily a Bose reaction where an α-haloketone and a suitable thiosemicarbazide derivative are introduced into the reaction. In addition, α-halohydrins and π-acceptors were used as C+-C+ synthons to obtain thiadiazines. Chloroacetic aldehydes synthesized by us are of undoubted interest for the preparation of functionalized 1,3,4-thia-diazines by the Bose reaction as synthetic equivalents of the two-carbon synthon C^+-C^+.

Despite the fact that numerous works have been devoted to the interaction of thiosemicarbazide with α-halocarbonyl compounds [1-4], it is practically impossible to predict the structure of the condensation

product with any α-halocarbonyl compounds. An analysis of the literature data shows that the products of such reactions, depending on the nature of the substituents in the α-halocarbonyl compound and the reaction conditions (temperature, medium, order of addition of reagents, etc.), can be thiadiazines [5], thiazoles [6], thiazolines [7], pyrazoles [8], and other compounds [1-4]. In a number of cases, with a change in the acidity of the medium, the products of the first stage of the reaction were isolated and identified: in a neutral medium, isothiocarbohydrazides [9] formed by alkylation at the sulfur atom; in a slightly acidic medium, α-halogenthiocarbazones [10] as a result of the Schiff reaction at the carbonyl group.

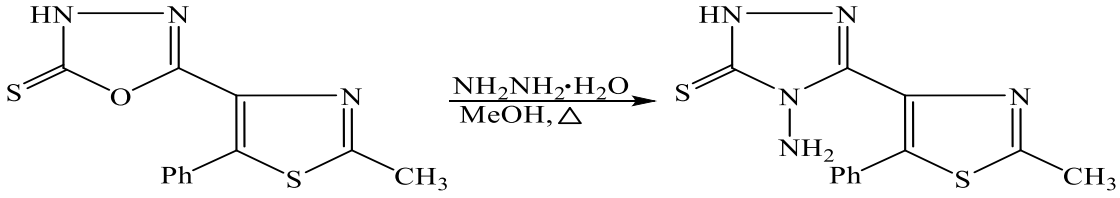
Phosphorylated α-haloacetic aldehydes in analogous cyclocondensations have not been studied. Therefore, we carried out these studies in detail on the example of the reactions of chloraldehydes with thiosemicarbazide, the results of which were reported in [11].

Triazolothiadiazines are of great interest as substances with antibacterial, antifungal and other types of biological activity. The main method for the synthesis of such compounds is the interaction of 3-mercaptotriazoles with various bifunctional nucleophiles, which proceeds, as a rule, in several stages with the release of side adducts and compounds. An analysis of the literature data shows that cyclic analogs of thiosemicarbazide, 4-amino-1,2,4-triazole-3-thiones, have recently been used in the synthesis of thiadiazine derivatives by a Bose-type reaction [12-15]. Only chloro- and bromoacetophenones and chloroacetone were used as α-halocarbonyl reagents in these reactions. Functionally substituted α-haloaldehydes have not yet been studied in such reactions.

Recently, in the practice of organic synthesis, 1,2,4-triazoles and their derivatives with a sulfur atom in the 3-position, 1,2,4-triazole-3-thiones, have been increasingly used. These five-membered heterocyclic compounds have a wide spectrum of biological activity, and also find application as effective additives to photographic materials and can be used as substances exhibiting insecticidal and herbicidal properties. Triazolethiones have two nucleophilic centers, an exocyclic sulfur atom and an endocyclic nitrogen atom, i.e., depending on the reaction conditions and the nature of the electrophilic substrate used, at the initial stage of the reaction, the sulfur atom or nitrogen atom of the heterocycle can play the role of the nucleophilic center. The participation of both nucleophilic centers in the reaction is not ruled out. Therefore, it can be said that the study of reactions of this kind of nucleophilic species with halocarbonyl compounds [13] can open up promising directions in organic synthesis, and can also lead to valuable intermediate products of organic synthesis.

Result and discussion

As a compound containing a thiosemicarbazide fragment, we used 3-thiazolyl-4-amino-1,2,4-triazole-5-thione substituted in the thiazolyl group, which was synthesized by us according to the well-known method by the reaction 2-(2'-methyl-5' -phenyl)-thiazolyl-1,3,4-oxadiazol-5-one with hydrazinhydrate. Boiling oxadiazole in methanol with a fivefold excess of hydrazine hydrate for five hours leads to 4-amino-1,2,4-triazole-5-thione in quantitative yield.



In contrast to the unsubstituted thiosemicarbazide, in 4-amino-1,2,4-triazole-5-thione the thiourea fragment responsible for the formation of five-membered heterocyclic systems is blocked in such a way that after the first stage the resulting intermediate (A) cannot be stabilized as a result of nucleophilic attack of nitrogen on the carbonyl carbon atom (path a) due to the absence of a proton at the attacking nitrogen atom.

At the same time, stabilization by means of an intramolecular Schiff reaction with the participation of an amine group (path b) is possible, especially since the presence of HCl in the form of a salt in the reaction mass should accelerate such a reaction.

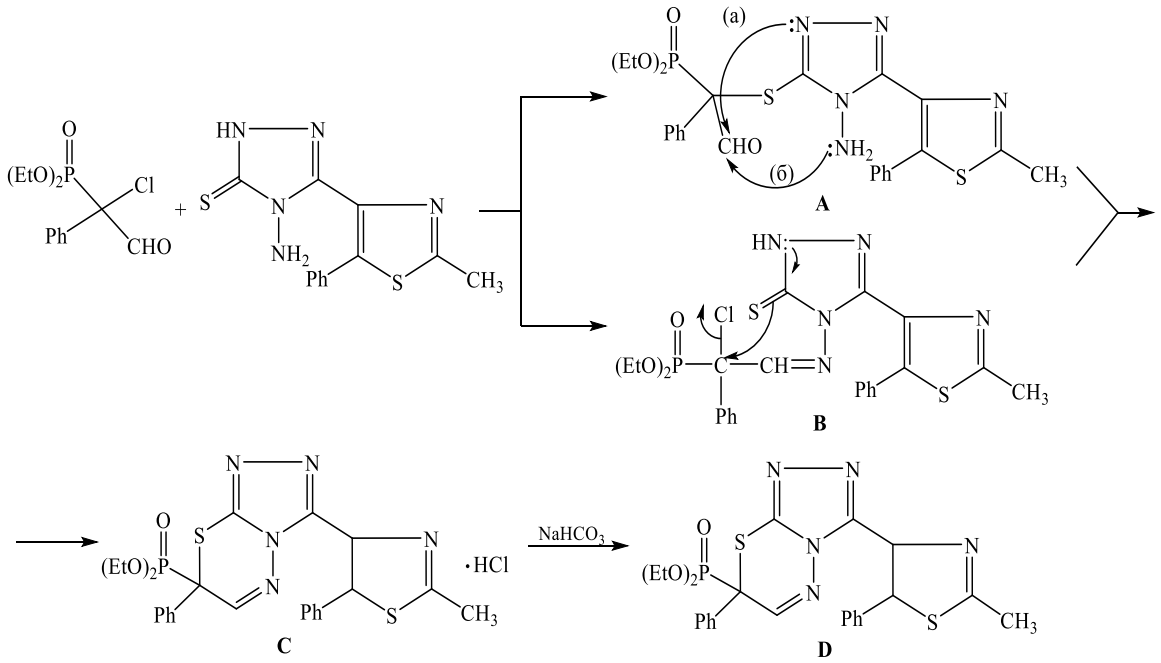


Table 1. Physicochemical characteristics and spectral data of the synthesized compound

Compound	Yield, %	T.m.p. °C	IR spectrum ν, см$^{-1}$	Spectrum NMR ^{31}P, ppm (85% H_3PO_4)	Spectrum PMR, δ, ppm, HMDS.	Found Calculated %			Formula
						N	P	S	
D*	80	184-186	780 (C-S) 1110(N-N) 1260-1280 (P=O) 1540 (Ph) 1640 (C=N)	25.7	1.10 (6H, t, $2CH_3$); 3.6 (3H, s, CH_3); 4.00 (4H, m, $2OCH_2$); 7.01-7.25 (10 H,m, 2 Ph); 7.8 (1H, d, =CH, $^3J_{PH}$=7.5 Hz) ($CDCl_3$).	13.18 13.33	5.83 5.9	12.28 12.19	$C_{24}H_{24}N_5O_3PS_2$

^{13}C {^{1}H}, *NMR($CDCl_3$+CCl_4): 19.96, 38.79, 53.99, 127.79, 129.06, 129.17, 129.70, 129.91, 130.09, 131.01, 134.87, 135.59, 140.41, 142.02, 145.55, 149.43, 161.64, 166.12.

The possibility of the formation of thiadiazine via the intermediate α-chlorothio-semicarbazone (B) cannot be ruled out either, which, being easily subjected to intramolecular nucleophilic substitution, can give the final product (D). Using only the data of elemental analysis, IR spectroscopy, and ^{1}H and ^{31}P NMR spectra, it is impossible to unequivocally answer the question about the structure of the product of the reaction of 3-thiazolyl-4-amino-1,2,4-triazolo-5-thione with aldehyde (4b). This problem was solved on the basis of mass spectroscopy data, which unambiguously identify the resulting compound as 3-thiazolyl-7-diethoxyphosphoryl-7-phenyl-1,2,4-triazolo[3,4 b]-1,3,4- thiadiazine.

Precise determination of ion masses shows the formation of a molecular ion with m/z 525 corresponding to the gross formula $C_{24}H_{24}N_5O_3PS_2$.

Experimental

Melting points are uncorrected and were recorded on SMP 30 apparatus. 1H NMR and 13C NMR spectra ware recorded on a 400 spectrophotometr using in $CDCl_3$+CCl_4 as the solvent. Chemical shifts values are reported in ppm taking tetramethylsilane as the internal standart and J values are given in hertz. The types of signals are indicated by the following letters: s=singlet, d=doublet, t=triplet, m=multiplet. Reactions were monitored by

thinlayer chromotography (TLC) using precoated silica gel plates, visualized by UV light.

3-(2'-methyl-5'-phenylthiazolyl-4'-yl)-4-amino-4H-1,2,4-triazolo-5-thione (known technique). To a solution of 3.28 g (0.012 mol) 2-(2'-methyl-5'-phenyl) thiazolyl-1,3,4-oxadiazol-5-one in 20 ml of methanol added 5 g (0.06 mol) of 60% hydrazine hydrate.

3-(2'-methyl-5'-phenylthiazolyl-4'-yl)-7-diethoxyphosphoryl-7-phenyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazine. A mixture of 2.91 g (0.01 mol) of chloraldehyde (46) and 2.89 g (0.01 mol) of 3-(2'-methyl-5'-phenylthiazolyl-4'-yl)-4-amino-4H-1,2,4-triazolo-5-thiona is boiled for 6 hours in absolute methanol. After cooling the reaction mixture to room temperature and evaporating the solvent, the resulting semicrystalline mass (123) is treated with 5% aqueous NaHCO3 solution, filtered, washed with water, dried and recrystallized from i-PrOH. The yield of 1,3,4-thiadiazine (124) was 4.2 g (80%).

References:

1. Kol`ceva, S.V., Andronnikova, G.P., & Mokrushin, V.S. (1991). "1,3,4-Tiadiaziny: metody sinteza i reakcionnaja sposobnost`". *HGS*, №4, pp. 435-448.
2. Novikova, A.P., Perova, N.M., & Chupahin, O.N. (1991). "Sintez i svojstva funkcional`nyh proizvodnyh 1,3,4-tiadiazinov i kondensirovannyh sistem na ih osnove". *HGS*, №11, pp.1443-1457.
3. Beyer, H. (1976). Quart. Reports on Sulfur *Chem.*, v. 318, p.971.
4. Beyer, H. (1969). 1,3,4-Thiadiazines. Z. *Chem.*, Bd. 9, No 10, pp.361-369.
5. Campaigne, E., & Selby, T. (1978). "Thiazoles and thiadiazines. The condensation of ethyl 4-chloroacetoacetate with thiosemicarbazide". *J. Heterocyclic Chem.*, v. 15, pp.401-411.
6. Asadov, H.A. (2018). "Sintez i geterociklizacija funkcionalizirovannyh α-tiocianatokarbonilnyh soedinenij". *Zhurnal himicheskih problem*, Baku, №3, pp. 400-419.
7. Bose, P., & Nandi, B. (1930). Thiadiazines. VI. *J. Ind. Chem. Soc.*, No 7, pp.733-739.
8. Beyer, H., Honenck, H., & Reichelt, L. (1970). "Zur reaktivitat von 2-dimethylamina-1,3,4-thiadiazinen". *Lieb. Ann.*, Bd. 741, pp.45-54.
9. Kol`ceva, S.V., Andronnikova, G.P., & Mokrushin, V.S. (1991). "1,3,4-Tiadiaziny: metody sinteza i reakcionnaja sposobnost`". *HGS*, №4, pp. 435-448.
10. Busby, R., & Dominey, T. (1980). "The rearrangement of 2-amino-1,3,4-thiadiazines to 3-amino-2-thiazolimines. Part I. The rates of rearrangement of a series of 5-alkyl- and 5-aryl-2-amino-1,3,4-thiadiazines at 30 and 50°C". *J. Chem. Soc. Perkin Trans.* II., v. 6, pp.890-899.
11. Beyer, H., & Wolter, G. (1658). Uber thiazole, XXIX. *Chem. Ber.*, Bd. 89, No 7, pp.1652-1658.
12. Asadov, H.A., Burangulova, R.N., & Gusejnov, F.I. (2003). "6-Fosforil-1,3,4-tiadiaziny". *HGS*, №5, pp.772-773.
13. Nurhametova, I.Z. (2001). *"Sintez, getero- i karbociklizacija funkcional`no zameshhennyh tiazolidinov, tiazolov i 1,3,4-tiadiazinov:* diss. kand. him. Nauk". (p.154). Kazan`.
14. El-Khawase, S., & Habib, N. (1989). "Synthesis of 1,2,4-triazole, 1,2,4-triazolo-[3,4-b]1,3,4]-thiadiazole and 1,2,4-triazolo-[3,4-b][1,3,4]-tiadiazine derivatives of benzotriazoles". *J. Heterocyclic. Chem.*, v. 26, №1, pp.177-179.
15. Molina, P., Alajarin, M., & De Vega, I.P. (1855). "Synthesis of 6,7-dihydro-5H-1,2,4-triazolo-[3,4-b][1,3,4]-thiadiazines by a C-C ring ciclization under mild conditions". *J. Chem. Soc., Perkin Trans* I, pp.1853-1855.