Chemistry of Heterocyclic Compounds, Vol. 44, No. 11, 2008

α-THIOCYANATOCARBONYL COMPOUNDS. 2.* CONDENSATION OF PHOSPHORYLATED α-PHENYL-α-THIOCYANATOACETALDEHYDE WITH PHOSPHORUS NUCLEOPHILIC REAGENTS

Kh. A. Asadov[1], G. G. Mikailov[2], S. N. Guseinova[2], R. N. Burangulova[1], R. J. Valiullina[1], A. M. Magerramov[2], and F. I. Guseinov[1]

We are the first to report a study of the reaction of phosphorylated α-phenyl-α-thiocyanatoacetaldehyde with triphenylphosphine, dimethylphenylphosphine, and diethylphosphorous acid, which yields bisphosphorylated 4,5-thioazolidines.

Keywords: dimethylphenylphosphine, diethylphosphorous acid, thiazolidine 4,5-bisphosphonate, triphenylphosphine, phosphorylated α-thiocyanatoaldehydes.

The properties of alkyl and aryl thiocyanates have been studied rather extensively in light of the insecticidal activity of some of these compounds [2]. The synthetic methods for various thiocyanate derivatives are based, as a rule, on the reaction of the corresponding halides, sulfates, or sulfonates with ammonium or alkali metal thiocyanates [3-5]. Phosphorylated α-thiocyanatoaldehydes, whose synthesis was reported in our previous work [1], have considerable synthetic possibilities. These compounds are reagents for the preparation of a broad range of linear and cyclic N-, P-, and S-containing derivatives, which may also contain other heteroatoms. As a result of these synthetic uses and other practical applications, α-thiocyanatoacetaldehydes have attracted considerable interest.

The direction of the reactions of organic thiocyanates with P(III) derivatives is largely a function of the nature of the phosphorus reagent. The reaction may take place either heterolytically or homolytically. Thiocyanates may enter both substitution reactions (due to the pseudohalide properties of the cyano group) and addition or cycloaddition (due to the presence of a polarized triple bond) [6].

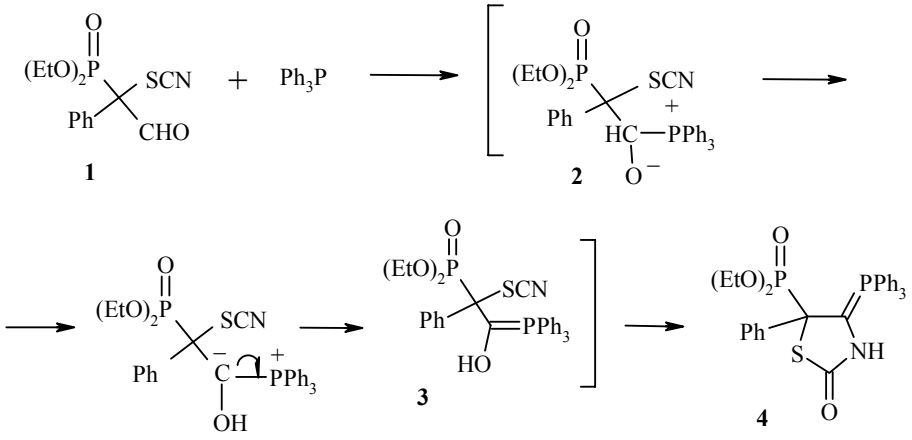
The adducts formed as the result of the addition of phosphines to nonconjugated carbonyl compounds are unstable due to the lack of possibility of delocalization of the negative charge. Thus, such addition reactions, which theoretically might proceed either at the oxygen atom or carbon atom of the carbonyl group, are reversible and the equilibrium is strongly shifted toward the starting compounds. However, the formation of stable compounds is possible when there is a subsequent reaction of the intermediate betaine with a second molecule of the carbonyl compound or some conjugated group.

* For Communication 1, see [1].

[1]Kazan State Technological University, Kazan 420015, Russia; e-mail: esedoglu@mail.ru. [2]Baku State University, Baku AZ-1148, Azerbaijan; e-mail: mikail05@mail.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1707-1711, November, 2008. Original article submitted November 6, 2007.

We have found that the reaction of thiocyanatoacetaldehyde **1** with triphenylphosphine proceeds over 18-25 h at reflux in an inert solvent such as benzene or toluene to give intermediates **2** and **3**. Subsequent cyclization of compound **3** occurs with the participation of the strongly polarized C≡N bond of the SCN group. The use of xylene as the solvent leads to tar formation.

A combined physicochemical and spectral study has shown that heterocyclization occurs in this reaction with the formation of a heterocyclic product **4**.



The IR spectrum of heterocycle **4** has a broad absorption band at 1177-1203 cm^{-1}, which is assigned to C=P bond stretching vibrations. The stretching band at 2120-2160 cm^{-1} characteristic for the SCN group and the OH group band at 3100-3500 cm^{-1} are lacking. The IR spectrum also has a C=O group band at 1722 cm^{-1} and a secondary amino group band at 2910 cm^{-1}. The ^1H NMR spectrum in acetone-d_6 has signals for the CH_3 group at 1.00 ppm and for the OCH_2 group at 4.00 ppm as well as a multiplet at 7.30-7.80 ppm (Ph, $^3J_{PH}$ = 10 Hz) and a broad singlet at 11.00 ppm for the NH proton with integral intensities 6:4:20:1.

All these data and the finding two resonance signals in the range 23.7 and 27.1 ppm in the ^{31}P NMR spectrum of the heterocycle **4** indicate that this reaction proceeds to give heterocyclic structure **4**.

The reaction of **1** with dimethylphenylphosphine proceeds analogously to give dimethylphenyl derivative **5**.

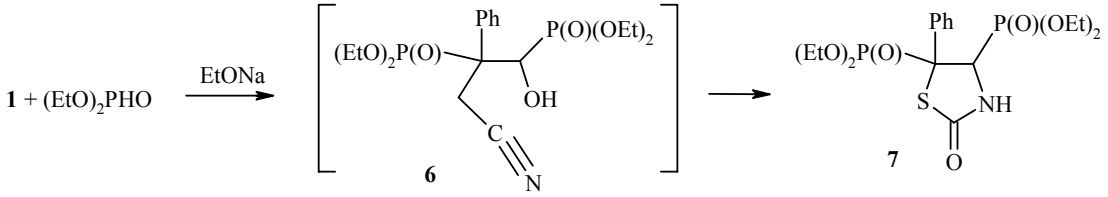
The ease of the reaction of aldehyde **1** with triphenylphosphine led us to study the behavior of its diacetal relative to Ph_3P. These studies showed that weakly nucleophilic triphenylphosphine is inert toward this acetal even upon prolonged heating at reflux.

An attempt to use BF_3 etherate in order to obtain S-(triphenyl)quasiphosphonium tetrafluoroborate also was unsuccessful even though the possible coordination of boron trifluoride at the –S–C≡N group might have been expected to polarize this moiety and permit attack of triphenylphosphine at the sulfur atom, i.e., BF_3 might have been expected to facilitate the electrophilic activation of the nucleophilic substitution. This failure is apparently due to steric factors of the sulfur atom itself and the three bulky substituents at the central carbon atom.

There is no information in literature on the reactions of thiocyanatocarbonyl compounds with diethylphosphorous acid. Hence, we tried to carry out the reaction of thiocyanate **1** with esters of trivalent phosphorus acids since alkyl thiocyanates are known to undergo the Arbuzov reaction with alkyl phosphites to give thiol phosphates [5, 7].

The reaction of aldehyde **1** with diethylphosphorous acid in the presence of sodium ethylate as catalyst gives O,O-diethyl(2-oxo-5-phenyl-4H-1,3-thiazolidine-4,5) bisphosphonate (**7**) in high yield (70%).

Addition of diethylphosphorous acid at the carbonyl group of compound **1** probably occurs in the first step, yielding intermediate adduct **6**, which undergoes intramolecular cyclization to form a thiazolidine ring **7**. The composition and structure of **7** were supported by elemental analysis and IR, ^{1}H, and ^{31}P NMR spectroscopy.



The ^{1}H NMR spectrum of heterocycle **7**, in addition to characteristic signals of the ethoxyl and phenyl fragments, has signals for the methine proton as a doublet of doublets at 5.20 ppm with $^{3}J_{PH}$ = 12.5 Hz and $^{3}J_{PH}$ = 20 Hz and a broad signal for the NH proton at 9.8 ppm. The ^{31}P NMR spectrum has phosphorus nuclear signals at 16.18 (br. s) and 23.52 ppm (d).

The IR spectrum of compound **7** has stretching bands for the following functional groups: 1017 (P–O–P), 1097 (P–O–P), 1261 (P=O), 1745 (C=O), 2962 cm^{-1} (NH). The reason for the shift of the P=O band (from 1280-1290 to 1261 cm^{-1}) and the NH band (from 3200-3300 to 2962 cm^{-1}) is attributed presumably to formation of a hydrogen bond between the P=O and NH groups due to the orientation of the phosphoryl group relative to the plane of the heterocycle.

The reaction schemes given above show that the reactions of phosphorylated thiocyanatoacet aldehyde **1** with phosphorus nucleophilic reagents, leading to heterocyclic products, have a common feature, namely, addition of the nucleophile at the carbonyl group and subsequent intramolecular heterocyclization involving the SCN group.

Thus, this first study of phosphorylated α-phenyl-α-thiocyanatoacetaldehyde with triphenylphosphine, dimethylphenylphosphine, and diethylphosphorous acid has yielded a promising approach for the preparation of new bisphosphorylated heterocycles with an unusual combination of substituents. These products hold promise as new types of ligands in the synthesis of organophosphorus metal complexes.

EXPERIMENTAL

The IR spectra were taken in vaseline mull or KBr pellets on a UR-20 spectrometer. The ^{1}H NMR spectra were taken on a Tesla BS-567 spectrometer at 200 MHz with HMDS as the standard. The ^{31}P NMR spectra were taken on a Bruker MSL-400 spectrometer at 162 MHz in 85% H_3PO_4 as the standard.

O,O-Diethyl 2-Oxo-5-phenyl-4-triphenylphosphinothiazolidine-5-phosphonate (4). A mixture of aldehyde **1** (3.13 g, 0.01 mol) and triphenylphosphine (2.62 g, 0.01 mol) was heated at reflux in toluene for 18 h. The solvent was removed in vacuum and the crystalline precipitate of heterocycle **4** was filtered off, washed with ether, and dried to give 4.0 g (70%) compound **4**, mp 157-158°C. IR spectrum, ν, cm^{-1}: 1177-1203 (C=P), 1280 (P=O), 1722 (C=O), 2910 (NH). ^{1}H NMR spectrum in acetone-d_6, δ, ppm (*J*, Hz): 1.00 (6H, m, 2CH_3); 4.00 (4H, m, 2OCH_2); 7.30-7.80 (20H, m, 4C_6H_5); 11.00 (1H, br. s, NH). ^{31}P NMR spectrum, δ, ppm: 23.7, 27.1. Found, %: N 2.48; P 10.69; S 5.63. $C_{31}H_{31}NO_4P_2S$. Calculated, %: N 2.43; P 10.78; S 5.57.

O,O-Diethyl 2-Oxo-4-dimethylphenylphosphino-5-phenylthiazolidine-5-phosphonate (5) was obtained analogously to compound **4** in 72% yield, mp >330°C. IR spectrum, ν, cm^{-1}: 1170-1195 (C=P), 1289 (P=O), 1710 (C=O), 2981 (NH). ^{1}H NMR spectrum in C_6D_6, δ, ppm (*J*, Hz): 1.05 (6H, m, 2CH_3); 1.4 (6H, d, $^{3}J_{PH}$ = 26, 2CH_3); 4.00 (4H, m, 2OCH_2); 7.3-7.5 (5H, m, C_6H_5); 8.2 (1H, br. s, NH). ^{31}P NMR spectrum, δ, ppm: 23.42, 29.84. Found, %: N 3.14; P 13.81; S 7.15. $C_{21}H_{27}NO_4P_2S$. Calculated, %: N 3.1; P 13.75; S 7.1.

O,O-Diethyl 2-Oxo-5-phenyl-4H-thiazolidine-4,5-bisphosphonate (7). A solution of diethyl phosphite (1.38 g. 0.01 mol) in ether (10 ml) was added with stirring to a mixture of aldehyde **1** (3.13 g, 0.01 mol), EtONa (0.3 g, 0.01 mol), and absolute ether (30 ml) at room temperature. Stirring was continued for 2 h at room temperature and 1 h at reflux. Then, 10 ml water was added to the reaction mixture. The ethereal layer was removed and the aqueous layer was extracted thrice with ether. The combined ethereal extracts were dried over $MgSO_4$. Removal of the solvent gave 3.16 g (70%) bisphosphonate **7** as an oil. IR spectrum, ν, cm^{-1}: 1017 (P–O–C), 1097 (P–O–C), 1261 (P=O), 1745 (C=O), 2962 (NH). ^{1}H NMR spectrum in acetone-d_6, δ, ppm (*J*, Hz): 1.00 (12H, m, $4CH_3$); 4.10 (8H, m, $4OCH_2$); 5.20 (1H, dd, $^3J_{PH}$ = 12.5, $^3J_{PH}$ = 20, CH); 7.10-7.50 (5H, m, C_6H_5); 9.8 (1H, br. s, NH). ^{31}P NMR spectrum, δ, ppm: 16.18, 23.52. Found, %: N 3.14; P 13.55; S 7.07. $C_{17}H_{27}NO_7P_2S$. Calculated, %: N 3.10; P 13.75; S 7.10.

This work was carried out with the financial support of the Russian Basic Research Fund (Grant No. 07-03-00316a) and the Russian Federation President's Grant MK-4043.2007.3.

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