Polish J. Chem., **75**, 1103–1119 (2001) **REVIEW ARTICLE**

Synthesis and Stereochemistry of Mono and Bicyclic 1,2-Thiaphosphacyclanes*

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(Received February 13th, 2001; revised manuscript April 10th, 2001)

The facile synthetic route to 5- and 6-membered mono and bicyclic 3-cyano-2-oxo-1,2-thiaphosphacyclanes has been elaborated on the base of intramolecular S-alkylation in a series of mono- and bis-ω-haloalkyl substituted thiophosphorylacetonitriles. The stereochemistry of the cyclic compounds was determined by NMR as well as X-ray diffraction. The diastereomeric transformations of 3-cyano-2-oxo-1,2-thiaphosphinanes and formation of conglomerates in the case of 6-cyano-2-oxa-10-thia-1-phosphabicyclo[4.4.0]decane-1-oxide are discussed.

Key words: S-alkylation, 3-cyano-2-oxo-1,2-thiaphospholane, 3-cyano-2-oxo-1,2-thiaphosphinane, 6-cyano-2-oxa-10-thia(oxa)-1-phosphabicyclo[4.4.0]decane-1-oxide

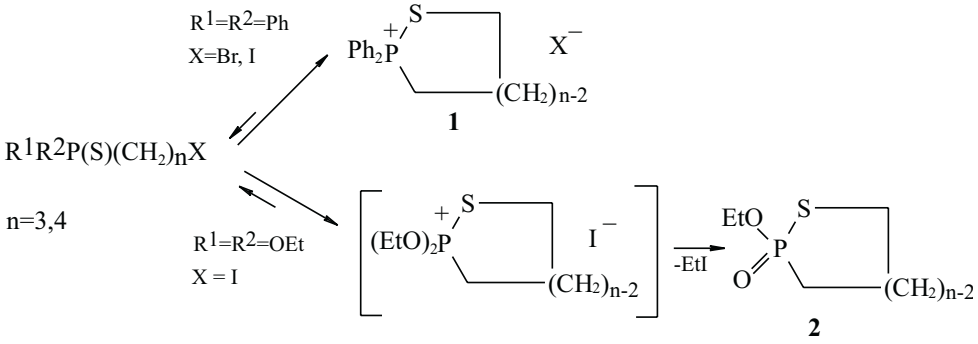
The chemistry of heterocyclic compounds is one of the most intensively developing fields of organic chemistry. This is apparently connected with high biological activity of numerous compounds of this type, some of them have already found application as medicines. Also, the same situation one may observe in the chemistry of organophosphorus compounds. Nowadays, the synthetic routes to phosphacyclanes [1], 1,3,2-diheteraphosphacyclanes [2–5] and non-saturated phosphorus containing heterocycles [6] have been rather well elaborated. Mainly, these methods are based on the interaction of different phosphorus chlorides with polynucleophilic reagents (polyatomic alcohols, thiols, amines, *etc*.). Among 1,2-monoheteraphosphacyclanes there are mostly known the corresponding compounds having oxygen as heteroatom. They are useful as noncombustible hydraulic liquids and plasticizers [7,8], flame retardants [9], thermostabilizing additives to fibers [10,11], surfactants [12] and so on. But in spite of being of undoubted interest, both from practical and theoretical point of view, only a few representatives of their analogues, having sulfur as heteroatom, were described, but none of them has any substituent in the ring (see, for example [13–17]).

Recently, it was shown in our laboratory [18–21] that non-functionalized ω-haloalkylsubstituted thiophosphoryl compounds easily undergo intramolecular S-alkyl-

* Dedicated to Prof. Jan Michalski on the occasion of his 80th birthday.

ation, yielding either 1,2-thiaphosphacyclanium salts **1** or, if there is the possibility of a subsequent dealkylation in an intermediate salt, 2-oxo-1,2-thiaphosphacyclanes **2** (so called thiolphostones) (Scheme 1).

Scheme 1

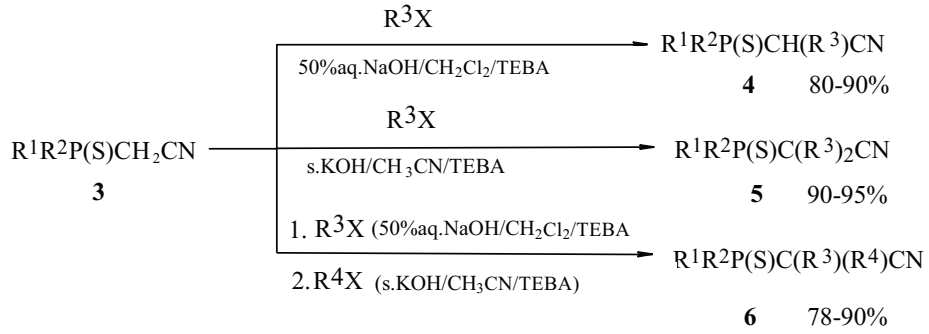


It should be noted, that subsequent functionalization of non-substituted 1,2-thiaphosphacyclanes, with the introduction of substituents to the ring, was a rather problematic task. However, such intramolecular S-alkylation represents apparently the general principle of 1,2-thiaphosphacyclane structure formation. Thus, in other words, starting from different thiophosphoryl compounds, bearing various functions and an ω-haloalkyl group in the molecule, one could obtain a variety of functionalized 1,2-thiaphosphacyclanes. This work concerns the cyclization of corresponding ω-haloalkylsubstituted thiophosphorylacetonitriles, wherein cyano group presents the above mentioned function. These compounds seemed to be the most attractive ones, since for them the dual reactivity on function *via* the course of cyclization was practically completely excluded.

Thus, the primary task of our investigation was to elaborate synthetic routes to previously unknown mono- and bis-ω-haloalkylsubstituted thiophosphorylacetonitriles. We intended to synthesize the desired compounds *via* an alkylation of thiophosphorylacetonitriles, using unsymmetric α,ω-dihaloalkanes. Note, that previously we have found [22,23] that one can achieve the high selectivity of mono- and dialkylation of starting thiophosphorylacetonitriles **3** by primary monohaloalkanes, using different interphasic systems. In other words, the result of the such alkylation depends on the PTC system in use (Scheme 2). Thus, monoalkylated thiophosphorylacetonitriles **4** were obtained in high yields using 50% aq. NaOH in dichloromethane solution, while application of solid KOH in acetonitrile leads to the dialkylated products **5**. The subsequent utilization of these two systems allows to obtain unsymmetric dialkylated compounds **6**.

Usually unsymmetric α,ω-dihaloalkanes react similar to primary monohaloalkanes at the site with higher electrophilicity. But surprisingly it was shown [23,24], that the result of their interaction with thiophosphorylacetonitriles under PTC conditions depends mainly on the alkylene chain length in electrophilic agent and reaction

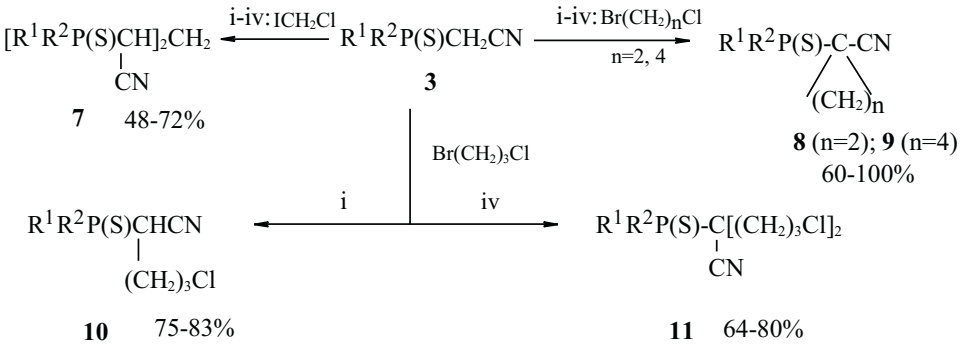
Scheme 2



R^1=R^2=Ph, OEt, O^{n}Pr, O^{n}Bu; R^1=Me, R^2=O^{i}Pr, O^{i}Bu; R^1=Ph, R^2=OEt; R^3, R^4=Me, Et, ^{n}Pr,^{n}Bu; X=Br, I.

conditions are responsible only for the yields of the major products. Thus, independently on the PTC system in the case of chloroiodomethane, the corresponding bis-phosphorylated glutaronitriles **7** were obtained as main reaction products. The reactions with 1,2-bromochloroethane and 1,4-bromochlorobutane proceeded according the cycloalkylation scheme and resulted in thermodynamically more stable gem-disubstituted cycloalkanes **8**,**9**. Only 1,3-bromochloropropane reacted similar to monohaloalkanes, what allowed us to obtain the corresponding C-mono and C,C-bis-3-chloropropylsubstituted compounds **10**,**11** in high yields (Scheme 3).

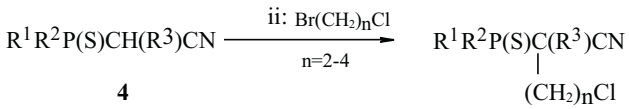
Scheme 3



R^1=R^2=Ph, OEt, O^{n}Pr, O^{n}Bu; R^1=Me, R^2=O^{i}Pr, O^{i}Bu; R^1=Ph, R^2=OEt;
i: 50%aq.NaOH/CH_2Cl_2/TEBA; ii: s.KOH/CH_3CN/TEBA;
iii: K_2CO_3/DMSO/TEBA; iv: 50%aq.NaOH/without solvent/TEBA;

Furthermore, C-alkyl-C-(ω-haloalkyl)derivatives **12** were obtained as the result of secondary alkylation of monoalkylated compounds **4** proceeded without any peculiarities (Scheme 4).

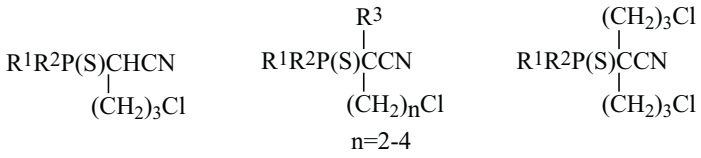
Scheme 4



R^1=R^2=Ph, OEt, O^{n}Pr, O^{n}Bu; R^1=Me, R^2=O^{i}Pr, O^{i}Bu; R^1=Ph, R^2=OEt; R^3= Me, Et, Pr, Bu

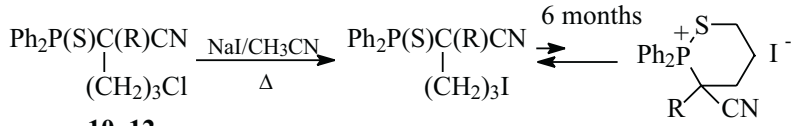
Also, to facilitate in some cases the subsequent intramolecular S-alkylation the analogues of compounds **10**, **11**, **12** with terminal iodine atom were obtained by the exchange reaction with sodium iodide in acetonitrile.

Thus, as a result of the study dealing with alkylation of thiophosphorylacetonitriles by unsymmetric α,ω-dihaloalkanes under PTC conditions, we succeeded to elaborate the facile synthetic approach to three types of the ω-haloalkylsubstituted compounds having cyano moiety shown below and further we investigated their reactivity.



It was shown that unlike non-functionalized ω-haloalkyl phosphine sulfides (X = Br, I), which spontaneously undergo intramolecular S-alkylation at storage or under reflux in acetone solution [18–20] yielding 1,2λ^5-thiaphosphacyclanium salts, their cyano-substituted analogues (bearing the diphenylthiophosphinyl group) are stable in the linear form and may be isolated. The corresponding cyclic phosphonium salts **13**,**14** were formed very slowly in acetonitrile solutions of **10**,**12** and in a few months the amount of **13**,**14** did not exceed 15% as measured by NMR technique (Scheme 5). Such lower reactivity could be easily explained by decreasing of thione sulfur atom nucleophilicity due to the introduction of electron withdrawing function into α-position.

Scheme 5



10, 12

13 - 15%
14 - 9%

10,13: R=H; **12,14:** R=Me

However, when compounds **10**,**12** have at least one alkoxy group at the phosphorus atom (cyano-substituted ω-haloalkylderivatives with thiophosphinate and thiophosphonate structure), the cyclization readily proceeded due to a subsequent irreversible

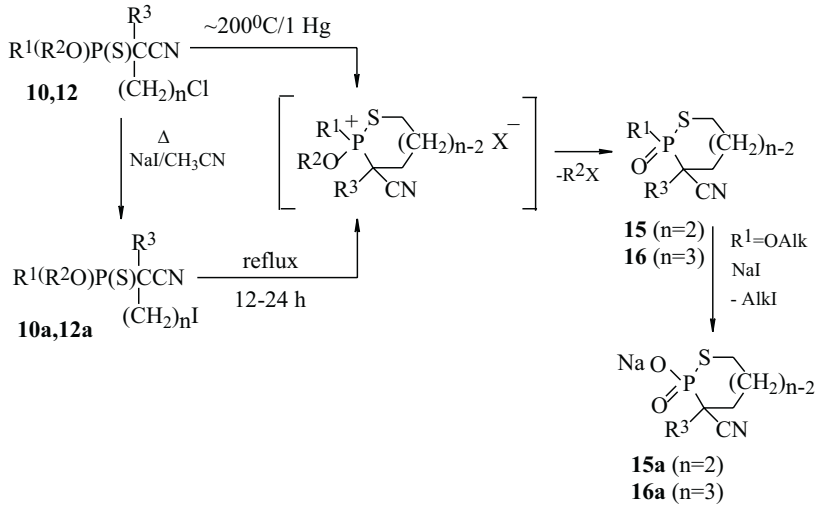
dealkylation in the intermediate thiaphosphocyclanium salt. Thus, the above compounds **10**,**12** with terminal chlorine atom partially transformed to the corresponding 5- and 6-membered thiolphostones **15**,**16** even being distilled *in vacuo*. It should be noted, that non-functionalized analogues of **10**,**12** bearing chlorine atom are thermally stable [20,21]. Thus, while introduction of cyano group decreases the thione sulfur nucleophilicity leading to reduction of the rate of phosphonium salt formation, at the same time it strongly promotes and facilitates the subsequent dealkylation process (Scheme 6). For such thermal cyclization the yield of cyclic compounds depends on the size of the resulting cycle, generally the cyclization to 5-membered derivatives proceeds more easily (Table 1). This dependence fits well with literature data [1,13,25] concerning the other phosphorus containing heterocycles. The yield is also influenced by the nature of radical R^2 in alkoxy group, which determines the ease of the dealkylation at the second step: the yield decreases with the elongation of this radical as well as passing from a primary alkyl group to a secondary one. To some extent the second radical R^1 at phosphorus also influences the yield. The starting compounds having alkyl subsituent R^3 were much more thermally stable, and in such case the yields of the 1,2-thiaphosphinanes **16** decreased drastically. This can be explained by steric hindrances in the transition state. To some extent the cyclization may be facilitated by addition of a catalytic amount of TEBA (Table 1).

Table 1. Dependence of yields of 3-cyano-2-oxo-1,2-thiaphosphacyclanes **15**,**16** on the starting compound structure **10**,**12** and method of cyclization.

#	R^1	R^2	R^3	n	Yield **15**,**16**, % ($NMR^{31}P$)	
					Distillation *in vacuo*	NaI/MeCN, reflux
1	EtO	Et	H	3	75	quant.[a]
2	PrO	Pr	H	3	55	32
3	Me	i-Pr	H	3	7	83
4	Me	i-Bu	H	3	30	53
5	Ph	Et	H	3	44[b]	79
6[c]	EtO	Et	Me	3	–	75
7	EtO	Et	Pr	3	15	30
8	PrO	Pr	Me	3	5.6(17[b])	28
9	Me	i-Bu	Me	3	–	64
10	Ph	Et	Me	3	19	quant.
11	EtO	Et	Me	2	19(40[b])	quant.[a]
12	Ph	Et	Me	2	–	61
13	Ph	Et	Et	2	95	100

[a] The cyclic sodium salt; [b] TEBA addition; [c] obtained from 3-bromopropyl thiophosphonate.

Scheme 6



R^1=OEt, OPr, Me, Ph; R^2=Et, Pr, i-Pr, i-Bu; R^3=H, Me, Et; n =2,3

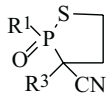
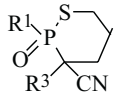
As one could expect, the cyclization of the corresponding iodo-derivatives obtained *in situ* proceeds under milder conditions. The conversion proceeds slowly at room temperature and the reaction is fully completed upon refluxing in acetonitrile during 12–24 hours (Scheme 6). It should be noted, that cyclization of corresponding thiophosphonates under these conditions (the excess of NaI) is accompanied by dealkylation of the second alkoxy group at the phosphorus atom, resulting in corresponding cyclic acid salts **15a**,**16a** in practically quantitative yields.

As cyano substituted thiolphostones **15**,**16** have two asymmetric atoms (phosphorus and carbon) and the above cyclizations are not stereoselective, in all cases these compounds were obtained as an equilibrium mixture of two diastereomers **A** and **B**, each being a racemic mixture of enantiomers. The ^{31}P-NMR spectra show two closely located signals (the diastereomer having a downfield signal was denoted as diastereomer **A**) (Table 2). The signals corresponding to 5-membered cycles **15** were registered at 65–73 ppm region, which is typical for phospholane species [1]. The chemical shifts in ^{31}P-NMR spectra of the 6-membered compounds **16** (35–52 ppm) have rather close values displaced upfield to the signals of linear structures with the same surroundings at the phosphorus. The difference between chemical shifts of the diastereomers ($\Delta\delta$) depends on size of the cycle, presence of alkyl substituent at 3 position and polarity of the solvent used.

The ratio of the diastereomers of compounds **15**,**16**, formed during the cyclization, is specified by the structure of the starting compound **10** or **12** (presence of the α-alkyl substituent) as well as method of cyclization and size of the cycle obtained (Table 2). For 2-alkoxy-2-oxo-1,2-thiaphosphinanes **16**, without the 3-alkyl substituent, the diastereomer ratio is 1:1, while for their 3-alkylsubstituted analogues the isomer **A** prevails when the cyclization is carried out *via* distillation *in vacuo*, but the

preferential formation of isomer **B** is usually observed under milder conditions of the cyclization (*via* the corresponding iodine derivatives).

Table 2. The ^{31}P-NMR data for 3-cyano-2-oxo-1,2-thiaphosphacyclanes **15**,**16** and dependence of diastereomer ratio on the method of cyclization.

		δ_P, ppm, ($CDCl_3$)		Ratio **A**:**B** Method of cyclization	
R^1	R^3	**A**	**B**	Distillation *in vacuo*	NaI/MeCN, reflux
				**15**	
OEt[a]	Me	69.62	68.12	**A** > **B** (60:40)	–
Ph	Et	72.71	65.11	**A** > **B** (70:30)	**A** < **B** (30:70)
Ph[a]	Me	71.79	65.56	–	**A** < **B** (40:60)
				**16**	
OEt	H	36.65	36.21	**A** ≈ **B**	**A** ≈ **B**
OPr	H	36.54	36.16	**A** ≈ **B**	**A** ≈ **B**
Me	H	41.99	39.38	**A** > **B** (60:40)	**A** < **B** (40:60)
Ph[b]	H	35.65	34.76	–	**A** ≈ **B**
OPr	Me	43.88	41.38	**A** >**B** (60:40)	**A** < **B** (40:60)
Ph	Me	44.47	40.54	–	**A** < **B** (40:60)
OEt	Pr	43.69	41.43	**A** > **B** (60:40)	**A** < **B** (30:70)
Me[b]	Me	51.67	47.45	–	**A** ≈ **B**
OEt	Me	43.93	41.51	–	**A** < **B** (40:60)

[a] Spectra were recorded in CH_2Cl_2; [b] in CD_3CN.

The compounds **15**,**16** were precipitated from distillates and reaction mixtures as solids upon ether addition with practically the same diastereomer ratio as that formed in the course of cyclization. In many cases the diastereomeric mixtures of **15**,**16** were resolved into the individual isomers using column chromatography or fractional crystallization. The structures of a series of the isolated individual diastereomers were thoroughly investigated by NMR (^{31}P, ^{1}H and ^{13}C) technique as well as X-ray diffraction analysis.

It is known that the assignment of isomer configuration for different types of phosphacyclanes is usually accomplished using proton NMR spectra. This method is based on the downfield shifted signals of all the kinds of protons in the *cis*-position to oxygen atom of the P=O group in comparison with those in *trans*-position [1,26]. The authors [26,27] used ^{13}C NMR spectra for the same purpose. However, we were not

sure that introduction of strong electron withdrawing cyano group would not break down the known dependences. Furthermore, for diastereomeric mixtures with **A**:**B** = 1:1 ratio it is impossible to compare the integral intensities in ^{1}H or ^{13}C NMR spectra with the ones in ^{31}P NMR spectra. It should be noted, that for the initial compounds **10**,**12** having two asymmetric centers, the change of the solvent often results in the change of the mutual signal positions of diastereomers **A** and **B** in ^{31}P NMR spectra. At the same time for the cyclic **15**,**16**, the mutual position of the signals, corresponding to stereoisomers **A** and **B**, remains unchangeable independently on the solvent in use, which is easy to follow by comparing their integral intensities. Such dependence remaining constant for a variety of solvents allow us to suggest ^{31}P NMR spectroscopy as simple and convenient method to control the stereochemical composition of the reaction mixtures and final products as well. But for such usage it was required to confront the chemical shift in ^{31}P NMR spectra of **15**,**16** with the structure of isomer according to X-ray diffraction data.

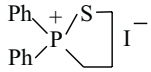
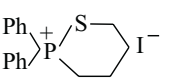
According to the X-ray data, CN group occupies an axial position in all compounds investigated. The bond lengths and bond angles in both 5- and 6-membered rings exhibit the expected values. The phosphorus atoms are characterized by a slightly distorted tetrahedral configuration. For **16** the P–S bond lengths vary in the narrow range (2.044–2.065 Å) and are similar to those in the series of 1,2λ^4-thiaphosphacyclanium salts [18,20]. These bond lengths are elongated for cyano substituted 5-membered cycles **15** and herein they vary in the range of 2.0751–2.0832 Å. The torsion angle O(1)P(1)C(4)C(5) is from 48.9 to 55.2° in the isomers with synclinal disposition of phosphoryl oxygen and CN group (*cis*-isomer) and from 147.6 to 170.6° in the case of periplanar disposition of these groups (*trans*-isomer). The selected bond lengths and bond angles for some 1,2-thiaphosphacyclanes with different substituents are shown in Table 3. Also there are presented comparison data obtained for non-functionalized 1,2-thiaphosphacyclanium salts [18–20].

As mentioned above, in all the molecules presented in Table 3 the P–S bond lengths are rather similar. Furthermore, in the 6-membered compounds with methyl group at the phosphorus atom S–C bond is significantly elongated and also very similar to the one in the structure of 1,2-thiaphosphinanium salt. Thus, we believe that phosphorus atom in cyano substituted thiaphosphocyclanes **15**,**16** is characterized by a significant positive charge, which is larger in the case of P-methyl derivative wherein the n-σ^* interaction (between sulfur electron lone pair and antibonded orbitals of the axial group) is less pronounced.

Comparison of the ^{31}P-NMR spectra and X-ray diffraction data allows to conclude that in the case of 2-oxo-1,2-thiaphosphinanes **16** diastereomer **A** with a downfield shift in its ^{31}P-NMR spectra is characterized by antiperiplanar disposition of cyano group and phosphoryl oxygen atom (*trans*) with the opposite configuration of the chiral centers (R^*_P,S^*_C), while the identical configuration of the asymmetric centers (R^*_P,R^*_C), with synclinal arrangement of above mentioned groups (*cis*) corresponds to diastereomer **B**. The only exception is 2-oxo-1,2-thiaphosphinanes with phenyl group at the phosphorus atom wherein the alteration of substituent precedence

leads to the identical configuration of the chiral centers in the *trans*-**A** isomer and to the opposite one in the *cis*-**B** isomer. On the contrary, in the case of 5-membered 1,2-thiaphospholanes **15** the isomer **A** having a downfield chemical shift is characterized by *cis* disposition of P=O and CN groups with identical configuration of chiral centres (R^*_P,R^*_C), while **B** isomer is the *trans* one with the opposite configuration of asymmetric atoms (R^*_P,S^*_C) (Fig. 1).

Table 3. Selected bond lengths (Å) and bond angles (°) for some 3-cyano-2-oxo-1,2-thiaphosphacyclanes **15**,**16**.

Diastereomer	P=O	P–S	P–C	S–C	S–P–C	O–P–C–C(N)
			1,2-thiaphospholanes **15**			
A (R^1=Ph, R^3=Et)[a]	1.4805	2.0751	1.869	1.840	95.84	165.4
		2.0832	1.873	1.834	97.87	147.6
B (R^1=Ph, R^3=Et)	1.478	2.0778	1.857	1.837	97.29	35.0
	–	2.068	1.805	1.850	100.1	–
			1,2-thiaphosphinanes **16**			
B (R^1=OEt, R^3=H)	1.456	2.044	1.817	1.807	99.2	48.9
B (R^1=OEt, R^3=Me)	1.467	2.056	1.836	1.832	99.54	55.2
A (R^1=Me, R^3=H)	1.488	2.062	1.838	1.838	97.2	170.6
B (R^1=Me, R^3=H)	1.484	2.065	1.833	1.833	100.13	50.0
B (R^1=Me, R^3=Me)	1.470	2.054	1.852	1.852	100.2	50.5
A (R^1=Ph, R^3=H)	1.477	2.059	1.839	1.827	99.1	170.0
	–	2.051	1.778	1.837	108.2	–

[a] Two independent molecules.

This dependence is further illustrated by particular examples. Thus, Fig. 2 and Fig. 3 demonstrate the general view of both isomers of 3-cyano-3-ethyl-2-oxo-2-phenyl-1,2-thiaphospholane **15**, while the structures of both isomers of 3-cyano-2-methyl-2-oxo-1,2-thiaphosphinane **16** according to the X-ray diffraction data are presented on Fig. 4 and Fig. 5. Therefore, ^{31}P NMR spectroscopy, which does not require chemically pure compounds, proved to be the simple and convenient method to determine the stereochemical structure of 3-cyano-2-oxo-1,2-thiaphosphacyclanes under investigation. The method may be used even for the estimation of the stereochemical composition of the reaction mixtures. We assume, that assignment of the configuration by NMR ^{31}P may be also used for the other similar heteraphosphacyclanes, provided that functional group in 3-position will occupy the axial position due to general anomeric effect.

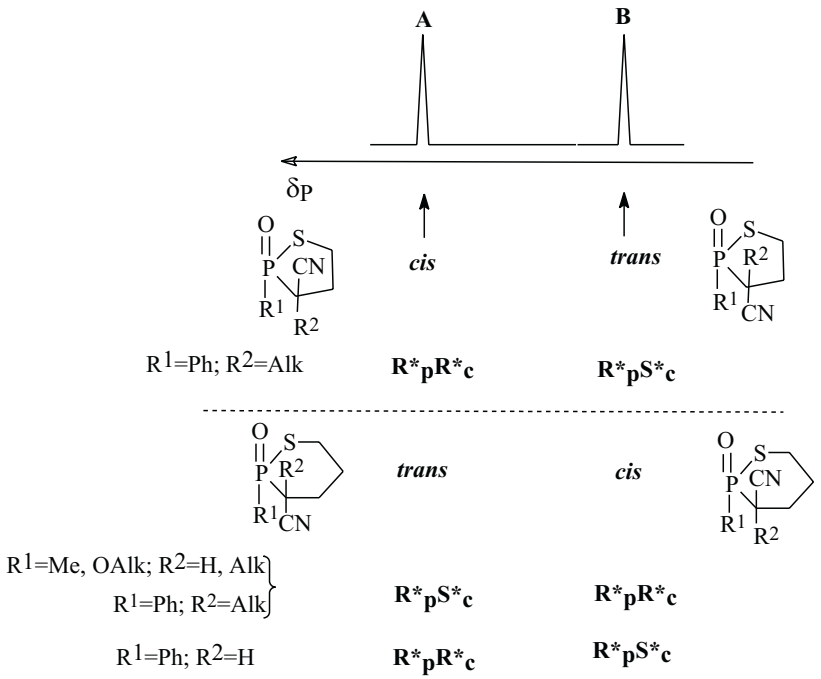


Figure 1. The structure of both stereoisomers of 6- and 5-membered 3-cyano-2-oxo-1,2-thiaphosphacyclanes.

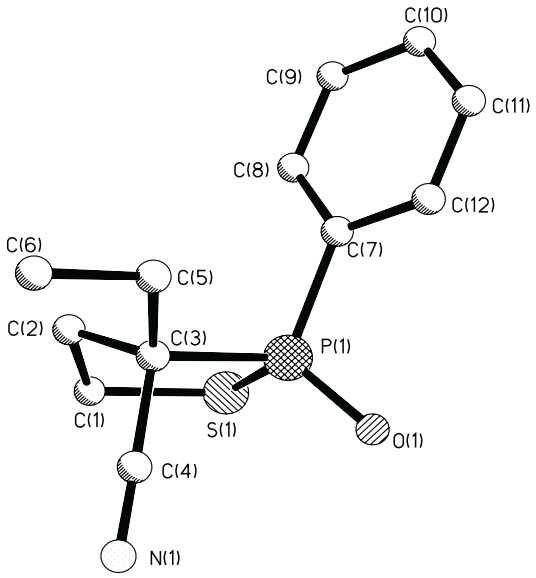


Figure 2. General view of **A**-*cis* diastereomer of 3-cyano-3-ethyl-2-oxo-1,2-thiaphospholane ($R^*_PR^*_C$).

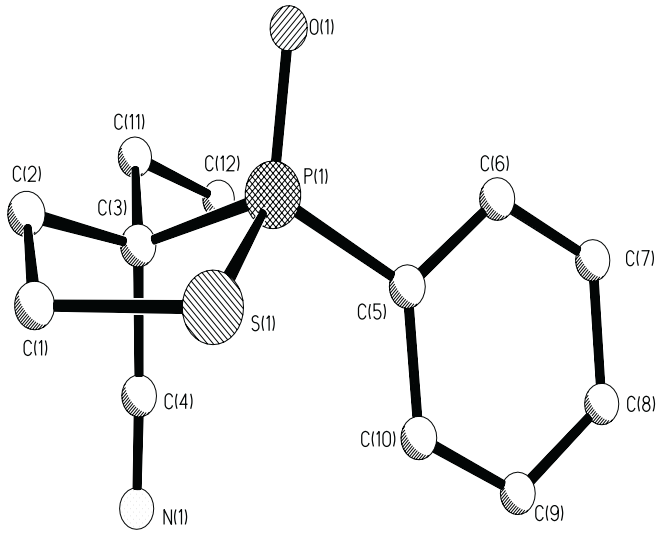


Figure 3. General view of **B**-*trans* diastereomer of 3-cyano-3-ethyl-2-oxo-1,2-thiaphospholane ($R^*_PS^*_C$).

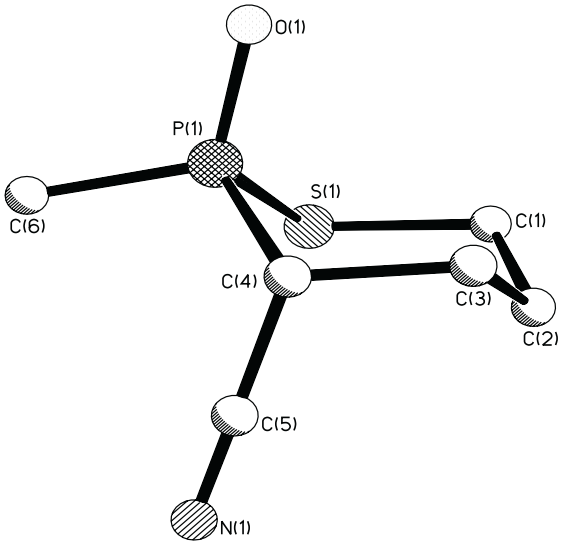


Figure 4. General view of **A**-*trans* diastereomer of 3-cyano-2-methyl-2-oxo-1,2-thiaphosphinane ($R^*_PS^*_C$).

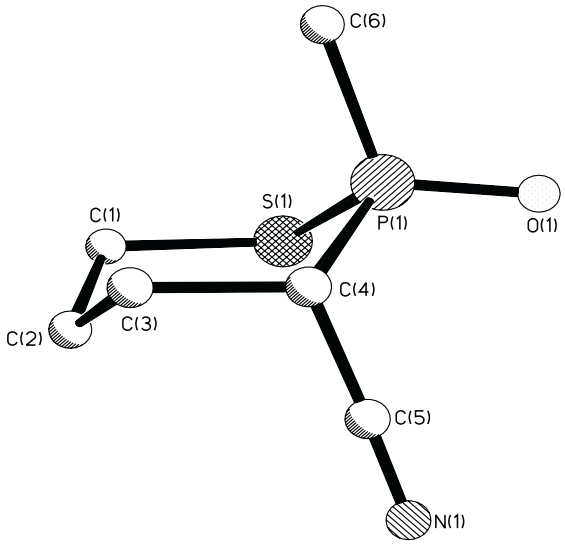
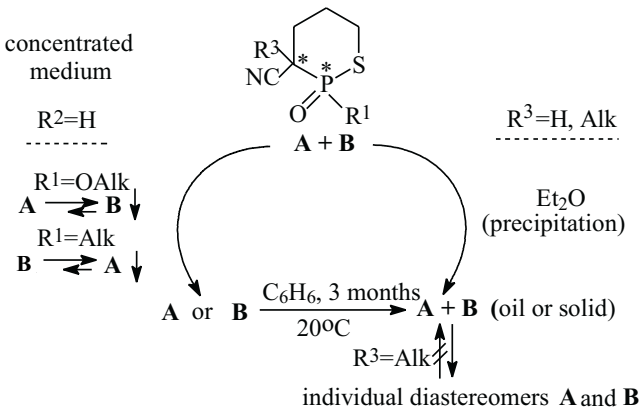


Figure 5. General view of **B**-*cis* diastereomer of 3-cyano-2-methyl-2-oxo-1,2-thiaphosphinane ($R^*_PR^*_C$).

For some cyclic compounds obtained, the diastereomeric transformations were found out [28]. Thus, in the case of 1,2-thiaphosphinanes **16** (without 3-alkyl substituent), the crude reaction products, representing the equilibrium mixtures of diastereomers, transformed slowly (without solvent) to a preferred individual diastereomer. The latter crystallized spontaneously from the mixture. The type of this preferred individual isomer depends on the substituent R^1 at the phosphorus atom (there were obtained the *cis*- isomer **B** when R^1 = OAlk and the *trans*-**A** one when R^1=Alk). Note, that in these preferred individual isomers the substituents at the phosphorus atom occupy the positions, which are the most advantageous in the view of general anomeric effect, *i.e*. the axial position is occupied by alkoxy group when R^1 = OAlk and by phosphoryl oxygen when R^1=Alk (Scheme 7). In benzene solutions the slow opposite conversion of the preferred diastereomer to the equilibrium mixture with initial statistical ratio of isomers was observed. It is interesting, that such transformations were not observed for the individual diastereomers of 3-alkyl substituted 1,2-thiaphosphinanes, which were isolated by fraction recrystallization. So, the possibility of reversible diastereomer transformations is apparently connected with the presence of the rather acidic hydrogen at the chiral 3-carbon atom of the cycle. That is to say, diastereomer conversions proceed *via* the dissociation of the above hydrogen atom, formation of a flat carbanion and subsequent hydrogen attachment with the configuration inversion of the asymmetric 3-carbon atom.

Scheme 7

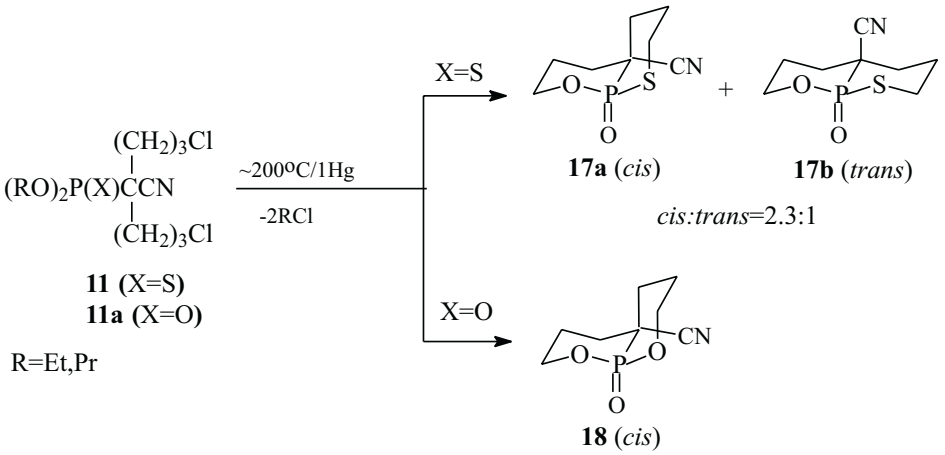


Also it should be noted that in crystals of the preferred stereoisomers obtained as a result of diastereomeric conversion molecules are assembled by H-bonds into centrosymmetric dimers, which in turn are interlinked by H-bonds into double layers. Evidently, the formation of such structure forming contacts of medium strength, according to the Desiraji classification [29], resulted in a crystallization of the preferred diastereomers from concentrated media, thereby shifting the equilibrium position. In other words, crystallization with the formation of the most advantageous crystal packing is the leading force of this process of diastereomeric transformations. In solutions, where there are no such contacts and H-bonds, the reverse conversion to the mixtures of diastereomers proceeds.

Further, we investigated the intramolecular cyclizations under distillation *in vacuo* in a series of bis(3-chloropropyl) thiophosphorylacetonitriles **11** and their analogues **11a.** Such type reactions proved to be the facile synthetic route to 6-cyanophosphabicyclodecane-1-oxides [30,31] (Scheme 8). The cyclization of **11** leads to the non-symmetric compound **17** with two different rings, namely 1,2-thia- and 1,2-oxaphosphinane ones, as a mixture of *cis* and *trans* isomers. When the substituted phosphorylacetonitrile **11a** was used as the starting material the *cis* isomer of the symmetric compound **18** with two 1,2-oxaphosphinane rings was obtained.

Till now three analogues of **18** were described having hydrogen, carboxy or methoxycarbonyl group in 6-position [32–35]. All these compounds were obtained by multistep procedures in rather low yields and all of them were obtained as *cis* isomers only. Also, there was reported [36] about the possibility to replace the phosphoryl oxygen in 2,10-dioxa-phosphabicyclo[4.4.0]decane-1-oxide by sulfur atom under the Lawesson's reagent action with the retaining of *cis* configuration. The exhaustive exchange of all oxygen atoms in the molecule of the former compound for sulfur (P_4S_{10}, Py) resulted in three sulfur containing 2,10-dithia-phosphabicyclo[4.4.0]decane-1-sulfide already as a mixture of *cis* and *trans* isomers in the 1.5:1 ratio.

Scheme 8



According to X-ray diffraction data (Fig. 6), 6-cyano-2,10-dioxa-phosphabicyclodecane-1-oxide **18** also consists of two *cis*-fused 6-membered rings both in chair conformation. Oxygen atoms are nonequivalent. Comparison with [32–34] for analogous compounds allows one to mention the simbate elongation of bridge P–C bond lengths with the increase of electron withdrawing character of 6-substitutent. According to the calculation by the molecular mechanics method using MMX force field, *cis*- is more thermodynamically preferable as compared with *trans*-**18**. However, the difference in energy is not very high (ΔE = 7.84 ccal per mole), therefore *trans* isomer is apparently less advantageous only because of the steric straining in the molecule (for example, between hydrogen atoms of different methylene groups in the rings).

As mentioned above, the corresponding sulfur containing compound **17** was obtained as a mixture of *cis* and *trans* isomers in 2.3:1 ratio. In this case the proportion of *trans* isomer is less than that for the above similar bicyclic compound with three sulfur atoms [36]. So, an introduction of the large sulfur atom to at least one 6-membered cycle instead of oxygen appears to decrease steric straining in *trans* isomer as a result of an elongation of the ordinary phosphorus-heteroatom bond.

Upon the addition of ether, the pure solid **17** precipitates from the distillates as a mixture of both isomers with the ratio *cis:trans* = 3.4:1. This mixture of isomers was separated into individual ones by column chromatography on silica gel. In addition, an enantiomeric composition of the above isomers was investigated in solutions by NMR-spectroscopy, using optically active l-phenylethylamine as the shift reagent. It was shown, that in course of cyclization both isomers were obtained as the statistical mixture of enantiomers (1:1). After chromatography separation the enantiomer ratio in *trans* isomer **17b** remained equal to 1:1. For *cis* isomer **17a** the enantiomer ratio varied in eluated fractions (from 1.5:1 to 1:1.5). After following crystallization of both individual isomers **17a**,**b** from benzene, the crystals of the *cis* isomer containing

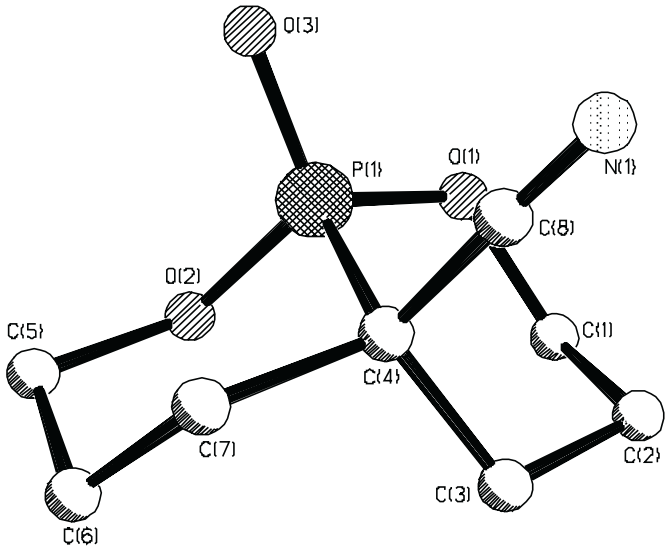


Figure 6. General view of *cis*-isomer of 6-cyano-2,10-dioxa-phosphabicyclodecane-1-oxide **18**. Selected bond lengths (Å): P(1)–O(3) 1.459(1), P(1)–O(1) 1.563(2), P(1)–O(2) 1.576(2), P(1)–C(4) 1.826(4); torsion angle O(3)P(1)C(4)C(8) = –42.96°.

enantiomers in 85:15 ratio and of the *trans* isomer with the ratio of enantiomers equal to 70:30 were obtained. Therefore, **17a**,**b** are conglomerates (mechanic mixture of enantiomeric crystals) undergoing the crystal induced spontaneous resolution (ee 70% and 40%, respectively). It should be noted that only five conglomerates of organophosphorus compounds are known according to [37], and only two of them were spontaneously resolved under crystallization.

The structures of **17a**,**b** have been confirmed by X-ray diffraction analysis**.** The general view, superposition of enantiomers and principal bond lengths for *cis*-**17a** are demonstrated on Fig. 7 (for the minor enantiomer only sulfur position is mentioned). Both asymmetric phosphorus and carbon atoms in the major enantiomer of **17a** have R configuration (as determined by Flack parameter). In Fig. 8 the superposition of two enantiomers for *trans*-**17b** is demonstrated according to the X-ray data. In the latter case, the X-ray parameters are not indicated, due to systematic errors introduced by superposition of enantiomers. In general, the geometry of both isomers of sulfur-containing phosphabicyclodecane **17** is close to that for the previously mentioned symmetric compounds.

In conclusion, the intramolecular S-alkylation presents a new general approach to 1,2-thiaphosphacyclane compounds, as exemplified by the study of intramolecular reactions in a series of thiophosphorylacetonitriles having ω-haloalkyl moiety. On this base, hitherto unknown cyanosubstituted mono- and bicyclic 1,2-thiaphosphacyclanes were obtained and investigated.

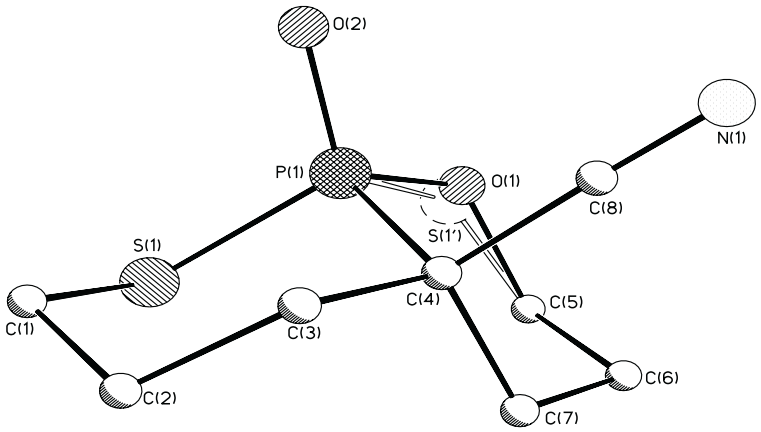


Figure 7. General view of *cis* 6-cyano-2-oxo-10-thia-phosphabicyclodecane-1-oxide **17a** and scheme illustrating the superposition of enantiomers. Selected bond lengths (Å): P(1)–O(2) 1.463(2), P(1)–O(1) 1.575(4), P(1)–S 2020(1), P(1)–C(4) 1.823(2); torsion angle O(2)P(1)C(4)C(8) = –48.4°.

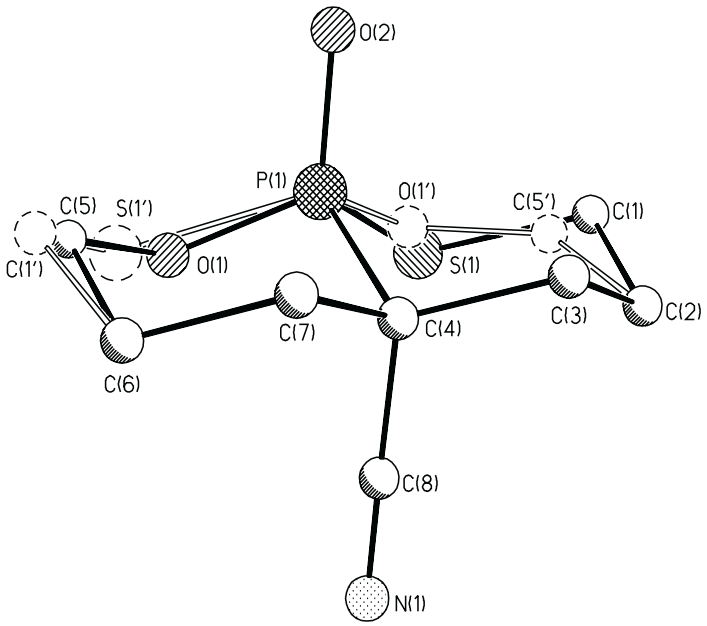


Figure 8. General view of *trans* 6-cyano-2-oxo-10-thia-phosphabicyclodecane-1-oxide **17b** and scheme illustrating the superposition of enantiomers. Torsion angle O(2)P(1)C(4)C(8) = 179°.

Acknowledgment

This work was supported by the Russian Foundation for Basic Research (grants no. 99-03-33014 and 00-15-97386).

REFERENCES

1. Quin L.D., The Heterocyclic Chemistry of Phosphorus Systems Based on the Phosphorus-Carbon Bond. Wiley-Interscience, 1981.
2. Pudovik M.A., Cherkasov R.A., Ovchinnikov V.V. and Pudovik A.N., *Usp. Khim*., **51**(8), 1305 (1982).
3. Pudovik M.A., Ovchinnikov V.V. and Cherkasov R.A., *ibid*., **52**(4), 640 (1983).
4. Polezhaeva N.A. and Cherkasov R.A., *ibid*., **54**(11), 1899 (1985).
5. Polezhaeva N.A. and Cherkasov R.A., *ibid*., **56**(2), 287 (1987).
6. Mironov V.F., Pudovik M.A. and Sinyashin O.G., *Zhurn. Rus. Khim. Obch*., **69**(1), 13 (1999).
7. Garner A.Y., Pat.US 2916510; *C. A*., **54**, 5571 (1960).
8. Garner A.Y., Pat.US 2953591; *C. A.*, **55**, 5347 (1961).
9. Kleiner H., Finke M., Bollert U. and Herwig W., *Pat. DE* 2346787 (1975); *C. A*., **83**, 44266 (1975).
10. Matsumoto T., Kanatsuki O. and Hamada S., *Jpn. Kokai Tokkyo Koho Yp* 63280728; *C. A*., **111**, 40152 (1989).
11. Ueda A. and Matsumoto T., *Jpn. Kokai Tokkyo Koho* Yp 62185710; *C. A*., **108**, 96114 (1988).
12. Germanaud L., Brunel. S. Chevalier Y. and Le Perchec P., *Bull. Soc. Chim. Fr.*, 699 (1988).
13. Chaundry A., Harger M.J.P., Stuff P. and Thompson A., *J. Chem. Soc. Chem. Commun*., 83 (1995).
14. Mathey F. and Thavard D., *J. Organomet. Chem*., **117**, 377 (1976).
15. Arbuzov B.A., Nikonova L.Z. and Nuretdinova O.N., *Izv. AN USSR*, *Ser. khim*., 648 (1973).
16. Uhing E.H., Pat US 4231970, *C. A*., **94**, 84303 (1981).
17. Uhing E.H., Pat US 4540526, *C. A*., **94**, 84303 (1981).
18. Aladzheva I.M., Bykhovskaya O.V., Lobanov D.I., Lyssenko K.A., Shishkin O.V., Antipin M.Yu., Struchkov Yu.T., Mastryukova T.A. and Kabachnik M.I., *Mend. Commun*., 58 (1996).
19. Lobanov D.I., Aladzheva I.M., Bykhovskaya O.V., Petrovskii P.V., Lyssenko K.A., Antipin M.Yu., Mastryukova T.A. and Kabachnik M.I., *Phosphorus*, *Sulfur and Silicon*, **128**, 145 (1997).
20. Aladzheva I.M., Bykhovskaya O.V., Lobanov D.I., Petrovskii P.V., Lyssenko K.A., Antipin M.Yu., Mastryukova T.A. and Kabachnik M.I., *Zhurn. Obsch. Khim*., **68**(9), 1421 (1998).
21. Mastryukova T.A., Aladzheva I.M., Lobanov D.I., Bykhovskaya O.V., Petrovskii P.V., Lyssenko K.A. and Kabachnik M.I., *Phosphorus*, *Sulfur and Silicon*, **144**–**146**, 569 (1999).
22. Odinets I.L., Vinogradova N.M., Artyushin O.I., Kalyanova R.M., Lyssenko K.A., Petrovskii P.V., Mastryukova T.A. and Kabachnik M.I., *Izv. AN*, *Ser. khim*., 990 (1998).
23. Vinogradova N.M., Odinets I.L., Artyushin O.I., Lyssenko K.A., Petrovskii P.V. and Mastryukova T.A., *Phosphorus*, *Sulfur and Silicon*, **144**–**146**, 589 (1999).
24. Vinogradova N.M., Odinets I.L., Artyushin O.I., Petrovskii P.V., Lyssenko K.A., Antipin M.Yu. and Mastryukova T.A., *Zhurn. Obsch. Khim*., **68**(9), 1434 (1998).
25. Aksnes G. and Bergessen K., *Acta Chem. Scand*., **20**, 2508 (1966).
26. Wroblewski A.E., *Tetrahedron*, **39**, 1809 (1983).
27. Thompson C.M., Frick J.A. and Green D.L., *J. Org. Chem*., **55**(1), 111 (1990).
28. Odinets I.L., Vinogradova N.M., Artyushin O.I., Petrovskii P.V., Lyssenko K.A., Antipin M.Yu. and Mastryukova T.A., *Mendeleev Commun*., 158 (1999).
29. Desiarju G.R., *Acc. Chem. Res*., **29**, 441, 1996.
30. Vinogradova N.M., Lyssenko K.A., Odinets I.L., Petrovskii P.V., Mastryukova T.A. and Kabachnik M.I., *Phosphorus*, *Sulfur and Silicon*, **132**, 265 (1998).
31. Odinets I.L., Vinogradova N.M., Lyssenko K.A., Petrovskii P.V. and Mastryukova T.A., *Heteroatom Chem*., **11**, 163 (2000).
32. Bellard S., Postle S. and Sheldrick G.M., *Acta Cryst. B*, **34**, 1032 (1978).
33. Cremer S.E., Sommese A.G. and Rodriques O., *Phosphorus*, *Sulfur and Silicon*, **75**, 107 (1993).
34. Lane T., Rodriques O.P., Tasz M.K., Sommese A.G. and Cremer S.E., *Phosphorus*, *Sulfur and Silicon*, **102**, 115 (1995).
35. Lane T., Rodriques O.P. and Cremer S.E., *Phosphorus*, *Sulfur and Silicon*, **103**, 63 (1998).
36. Polosov A.M. and Cremer S.E., *Phosphorus*, *Sulfur and Silicon*, **147**, 335 (1998).
37. Jacques J., Collet A. and Wilen S.M., Enantiomers, Racemates, and Resolutions. Krieger Publ. Comp., Malabar, Florida, 1994.